FILE 'HOME' ENTERED AT 08:15:26 ON 20 APR 2005

=> fil .bec

COST IN U.S. DOLLARS

SINCE FILE TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21 0.21

FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS, ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 08:15:52 ON 20 APR 2005 ALL COPYRIGHTS AND RESTRICTIONS APPLY. SEE HELP USAGETERMS FOR DETAILS.

11 FILES IN THE FILE LIST

=> s peg or polyethylene glycol

FILE 'MEDLINE'

8959 PEG

33678 POLYETHYLENE

22000 GLYCOL

9086 POLYETHYLENE GLYCOL

(POLYETHYLENE (W) GLYCOL)

L1 14753 PEG OR POLYETHYLENE GLYCOL

FILE 'SCISEARCH'

14973 PEG

49789 POLYETHYLENE

36174 GLYCOL

11455 POLYETHYLENE GLYCOL

(POLYETHYLENE (W) GLYCOL)

L2 21749 PEG OR POLYETHYLENE GLYCOL

FILE 'LIFESCI'

2228 PEG

4480 "POLYETHYLENE"

5906 "GLYCOL"

3000 POLYETHYLENE GLYCOL

("POLYETHYLENE" (W) "GLYCOL")

L3 4068 PEG OR POLYETHYLENE GLYCOL

FILE 'BIOTECHDS'

6044 PEG

3945 POLYETHYLENE

4515 GLYCOL

3036 POLYETHYLENE GLYCOL

(POLYETHYLENE (W) GLYCOL)

L4 7723 PEG OR POLYETHYLENE GLYCOL

FILE 'BIOSIS'

11854 PEG

23925 POLYETHYLENE

32559 GLYCOL

14532 POLYETHYLENE GLYCOL

(POLYETHYLENE (W) GLYCOL)

L5 20621 PEG OR POLYETHYLENE GLYCOL

FILE 'EMBASE'

8915 PEG

18670 "POLYETHYLENE"

28246 "GLYCOL"

8533 POLYETHYLENE GLYCOL

("POLYETHYLENE"(W) "GLYCOL")

L6 14197 PEG OR POLYETHYLENE GLYCOL

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FILE 'HCAPLUS'
         31703 PEG
        323028 POLYETHYLENE
        328789 GLYCOL
         90639 POLYETHYLENE GLYCOL
                  (POLYETHYLENE (W) GLYCOL)
L7
        108449 PEG OR POLYETHYLENE GLYCOL
FILE 'NTIS'
           321 PEG
          5591 POLYETHYLENE
          1894 GLYCOL
           253 POLYETHYLENE GLYCOL
                 (POLYETHYLENE (W) GLYCOL)
L8
           499 PEG OR POLYETHYLENE GLYCOL
FILE 'ESBIOBASE'
          3672 PEG
          4796 POLYETHYLENE
          6391 GLYCOL
          3005 POLYETHYLENE GLYCOL
                  (POLYETHYLENE (W) GLYCOL)
L9
          5248 PEG OR POLYETHYLENE GLYCOL
FILE 'BIOTECHNO'
          2816 PEG
          4665 POLYETHYLENE
          7260 GLYCOL
          3167 POLYETHYLENE GLYCOL
                  (POLYETHYLENE (W) GLYCOL)
L10
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FILE 'WPIDS'
         15802 PEG
        197943 POLYETHYLENE
        109036 GLYCOL
         26705 POLYETHYLENE GLYCOL
                  (POLYETHYLENE (W) GLYCOL)
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         39735 PEG OR POLYETHYLENE GLYCOL
TOTAL FOR ALL FILES
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         10817 CROSSLINK?
       1759365 PROTEIN#
        730058 ENZYME#
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FILE 'SCISEARCH'
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       1400079 PROTEIN#
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             3 L2 (5A) CROSSLINK? (5A) (PROTEIN# OR ENZYME#)
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FILE 'BIOTECHDS'

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FILE 'HCAPLUS'
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FILE 'BIOTECHNO'
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PROCESSING COMPLETED FOR L24
             32 DUP REM L24 (6 DUPLICATES REMOVED)
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L25 ANSWER 1 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
     Crosslinking of proteins and other biomolecules and organic molecules
ТT
     using metal coordination complexes and oxidizing agents
     PCT Int. Appl., 35 pp.
so
     CODEN: PIXXD2
IN
     Stewart, Russell John; Kiser, Patrick Franklin; Staynor, Richard Scott
AN
     2005:182803 HCAPLUS
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DN

142:276436

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APPLICATION NO.
                                     DATE
      PATENT NO.
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                                     20050303 WO 2004-US25958
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     WO 2005019421
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               SN, TD, TG
L25
     ANSWER 2 OF 32 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TТ
      Knot pusher for closing suture sites in body tissue, comprises body that
      engages suture knot, and fitting for introducing liquid closure material
      for discharge.
                        A1 20030227 (200358)*
                                                        37
PΙ
     US 2003040760
                                                               A61B017-04
                        A2 20040212 (200413) EN
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         RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
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              DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
              LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
              SE SG SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
     AU 2003269940
                        A1 20040223 (200453)
                                                               A61B017-04
     ADDIS, B; BROWNE, D; CHEUNG, D; HNOJEWYJ, O
IN
     ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
L25
      Chemical modification of enzymes to improve their catalytic performance
TI
SO
      Fenzi Cuihua (2002), 16(6), 475-480
      CODEN: FECUEN; ISSN: 1001-3555
ΑU
     Liu, Jian-zhong; Song, Hai-yan; Weng, Li-ping; Ji, Liang-nian
ΑN
      2003:170509 HCAPLUS
      138:381181
DN
     ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
L25
      Preparation of protein-based PEG hydrogels
TI
      PCT Int. Appl., 63 pp.
SO
      CODEN: PIXXD2
IN
      Faure, Marie-pierre; Pinard, Karl; Brisson, Jean-francois
AN
      2001:747876 HCAPLUS
      135:294022
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      PATENT NO.
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                                    DATE
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                                                                            DATE
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                                    20011011
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               LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
               RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
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      EP 1280849
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     ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
L25
```

TI Delivery systems using preformed biodegradable polymer compositions including crosslinked proteins

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SO
     PCT Int. Appl., 45 pp.
     CODEN: PIXXD2
     Truong, Myhanh T.; Pournoor, Kaveh; Choi, Hye-Ok; Velasquez, David J.;
IN
     Ferber, Richard H.; Bernatchez, Stephanie F.
     2001:617791 HCAPLUS
AN
     135:200442
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     PATENT NO.
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                         A2
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                                20010823
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     WO 2001060335
                         A3
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                                20030729
                                            JP 2001-559433
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                                                                   20010216
    ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
L25
     Peptide and protein PEGylation. A review of problems and solutions
TI
SO
     Biomaterials (2001), 22(5), 405-417
     CODEN: BIMADU; ISSN: 0142-9612
ΑU
     Veronese, F. M.
AN
     2001:23413 HCAPLUS
DN
     134:315938
    ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
L25
     Protein release from physically crosslinked hydrogels of the PLA/PEO/PLA
TI
     triblock copolymer-type
SO
     Biomaterials (2001), 22(4), 363-369
     CODEN: BIMADU; ISSN: 0142-9612
ΑU
     Molina, I.; Li, S.; Martinez, M. B.; Vert, M.
AN
     2000:891018 HCAPLUS
DN
     134:285525
    ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
L25
     Modification of Oligo(poly(ethylene glycol) fumarate) Macromer with a GRGD
ΤI
     Peptide for the Preparation of Functionalized Polymer Networks
SO
     Biomacromolecules (2001), 2(1), 255-261
     CODEN: BOMAF6; ISSN: 1525-7797
ΑU
     Jo, Seongbong; Shin, Heungsoo; Mikos, Antonios G.
ΑN
     2001:36321 HCAPLUS
DN
     134:252975
L25
    ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
     Protein-containing hydrogels
TΙ
SO
     Eur. Pat. Appl., 21 pp.
     CODEN: EPXXDW
     Ettner, Norbert; Schink, Michael; Schreiber, Joerg; Meier, Wolfgang;
IN
     Sauer, Marc
AN
     2000:553213 HCAPLUS
     133:155497
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     PATENT NO.
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                        A2
                               20000809
                                          EP 2000-100556
     EP 1025860
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                        A3
                               20020619
     EP 1025860
                         В1
                               20050112
           AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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                                        DE 1999-19903655
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                               20000810
L25 ANSWER 10 OF 32 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
     Barrier material, to close vascular puncture sites to prevent bleeding
     after surgery or trauma, comprises matrix of protein and polymer.
     WO 2000012018
                  A1 20000309 (200020)* EN 118 A61B017-36
PΙ
       RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
            OA PT SD SE SL SZ UG ZW
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           UA UG US UZ VN YU ZW
     AU 9955870
                    A 20000321 (200031)
                    A1 20010620 (200135) EN
     EP 1107813
                                                    A61M037-00
        R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI
     US 2001018598 A1 20010830 (200151)
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     US 2001031948
                   A1 20011018 (200166)
                                                    A61M005-178
     US 2002032463
                    A1 20020314 (200222)
                                                    A61D001-00
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     US 6371975
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     JP 2002525137
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     US 6458147
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     US 2002161399 A1 20021031 (200274)
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     CRUISE, G M; HNOJEWYJ, O; EDWARDS, S D; GOUGH, E
IN
    ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
L25
     Control and Prediction of Gelation Kinetics in Enzymatically Cross-Linked
TI
     Poly(ethylene glycol) Hydrogels
SO
     Macromolecules (2000), 33(15), 5476-5480
     CODEN: MAMOBX; ISSN: 0024-9297
ΑU
     Sperinde, Jeffrey J.; Griffith, Linda G.
     2000:453418 HCAPLUS
AN
DN
     133:177591
      ANSWER 12 OF 32 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
L25
TI
      Photoimmobilization of organophosphorus-hydrolase within a PEG-based
      hydrogel;
        effect of immobilization on crosslinked polyethylene
        glycol-based hydrogel support on enzyme activity and
        stability
SO
      Biotechnol.Bioeng.; (1999) 65, 5, 580-88
      CODEN: BIBIAU
                     ISSN: 0006-3592
ΑU
      Andreopoulos F M; Roberts M J; Bentley M D; Harris J M; Beckman E J;
      *Russell A J
      1999-14977 BIOTECHDS
ΑN
L25
     ANSWER 13 OF 32 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
      Optimization of Pseudomonas cepacia lipase preparations for catalysts in
TI
      organic solvents;
        transesterification
SO
      Biotechnol.Bioeng.; (1999) 62, 5, 554-61
      CODEN: BIBIAU
                      ISSN: 0006-3592
AU
      Secundo F; Spadaro S; Carrea G; Overbeeke P L
      1999-03096 BIOTECHDS
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ΑN

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ANSWER 14 OF 32
                         MEDLINE on STN
                                                         DUPLICATE 1
L25
     Chemical modification of enzymes for enhanced functionality.
ΤI
     Current opinion in biotechnology, (1999 Aug) 10 (4) 324-30. Ref: 41
so
     Journal code: 9100492. ISSN: 0958-1669.
ΑU
     DeSantis G; Jones J B
     1999380784
                    MEDLINE
AN
L25 ANSWER 15 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
     Crosslinked protein crystals as universal separation media
TI
SO
     PCT Int. Appl., 115 pp.
     CODEN: PIXXD2
     Margolin, Alexey L.; Vilenchik, Lev Z.
ΙN
     1998:208450 HCAPLUS
AN
DN
     128:267960
     PATENT NO.
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                                           APPLICATION NO. DATE
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     WO 9813119
                                          WO 1997-US17167 19970924
PΙ
                         A1 19980402
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             DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
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     AU 9747381
                          A1
                                 19980417
                                          AU 1997-47381
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    ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
L25
     Non-crosslinked protein particles for therapeutic and diagnostic use
TΤ
     U.S., 21 pp., Cont.-in-part of U.S. 5,616,311.
SO
     CODEN: USXXAM
     Yen, Richard C. K.
IN
AN
     1998:175365 HCAPLUS
DN
     128:235150
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     US 5725804
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     US 5308620
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                                                                    19940314
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                                20021003
                                            US 2002-42834
                                                                    20020108
      ANSWER 17 OF 32 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
L25
ΤI
      Enhancement of acid proteinase production by the fungus Humicola lutea
      120-5 immobilized in crosslinked poly(vinyl alcohol) mixed with
      poly(ethylene glycol);
         acid protease production following fungus immobilization
SO
      Process Biochem.; (1998) 33, 7, 725-28
      CODEN: PBCHE5
                      ISSN: 0032-9592
ΑU
      Alekseiva P; Petricheva E; Konstatinov H
```

1999-08447 BIOTECHDS

AN

- L25 ANSWER 18 OF 32 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
- TI MECHANICAL-PROPERTIES OF SOY PROTEIN-POLYETHYLENE RIBBON AND FILM EXTRUDATES
- SO TRANSACTIONS OF THE ASAE, (MAR/APR 1996) Vol. 39, No. 2, pp. 611-615. ISSN: 0001-2351.
- AU GHORPADE V M; HANNA M A (Reprint)
- AN 96:358795 SCISEARCH
- L25 ANSWER 19 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Crosslinked poly(ethylene glycol) networks as reservoirs for protein delivery
- SO Journal of Applied Polymer Science (1996), 59(3), 459-66 CODEN: JAPNAB; ISSN: 0021-8995
- AU Bromberg, Lev
- AN 1995:1004718 HCAPLUS
- DN 124:127031
- L25 ANSWER 20 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN

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- TI Sulfonamide derivatives and their use
- SO PCT Int. Appl., 74 pp.
  - CODEN: PIXXD2
- IN Baldwin, John J.; Ohlmeyer, Michael H. J.; Henderson, Ian

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- AN 1995:951322 HCAPLUS
- DN 123:350246

PA	TENT NO.		KIND	DATE	APPLICATION NO.	DATE
				10050014		10050310
PI WO					WO 1995-US3223	
	W: AM,	AT, AU,	BB,	BG, BR, BY,	CA, CH, CN, CZ, DE,	DK, ES, FI, GB,
	GE,	HU, JP,	KΕ,	KG, KP, KR,	KZ, LK, LT, LU, LV,	MD, MG, MN, MW,
	NL,	NO, NZ,	PL,	PT, RO, RU,	SD, SE, SI, SK, TJ,	TT, UA, US, UZ, VN
	RW: AT,	BE, CH,	DE,	DK, ES, FR,	GB, GR, IE, IT, LU,	MC, NL, PT, SE
CA	2183428		AA	19950914	CA 1995-2183428	19950310
AU	9519991		A1	19950925	AU 1995-19991	19950310
AU	690656		B2	19980430		
EP	751765		A1	19970108	EP 1995-913701	19950310
EP	751765		В1	20030507		
	R: AT,	BE, CH,	DE,	DK, ES, FR,	GB, GR, IE, IT, LI,	LU, MC, NL, PT, SE
	09510442		T2		JP 1995-523709	19950310
AT	239680		E	20030515	AT 1995-913701	19950310
ES	2199247		<b>T</b> 3	20040216	ES 1995-913701	19950310
US	5618825		Α	19970408	US 1995-482489	19950607
US	5756810		Α	19980526	US 1996-714065	19960911

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- L25 ANSWER 21 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Direct visualization of enzyme inhibitors using a portion mixing inhibitor library containing a quenched fluorogenic peptide substrate. Part 1. Inhibitors for subtilisin Carlsberg
- SO Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1995), (12), 1591-6 CODEN: JCPRB4; ISSN: 0300-922X
- AU Meldal, Morten; Svendsen, Ib
- AN 1995:647239 HCAPLUS
- DN 123:78136
- L25 ANSWER 22 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Densely crosslinked polymer networks of poly(ethylene glycol) in trimethylolpropane triacrylate for cell-adhesion-resistant surfaces
- SO Journal of Biomedical Materials Research (1995), 29(2), 207-15 CODEN: JBMRBG; ISSN: 0021-9304
- AU Drumheller, Paul D.; Hubbell, Jeffrey A.
- AN 1995:348766 HCAPLUS
- DN 122:114853

- L25 ANSWER 23 OF 32 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New active carbonate(s) of polyalkylene oxide(s) for modification of polypeptide(s).
- PI US 5324844 A 19940628 (199425)\* 10 C07D207-46
- IN ZALIPSKY, S
- L25 ANSWER 24 OF 32 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
- TI INTERACTIONS OF ENZYMES AND FUNGI WITH CROSS-LINKED POLYURETHANES PREPARED FOR BIOMEDICAL APPLICATIONS
- SO MEDICAL PROGRESS THROUGH TECHNOLOGY, (1994) Vol. 20, No. 3-4, pp. 261-270. ISSN: 0047-6552.
- AU JAYABALAN M (Reprint); SHUNMUGAKUMAR N
- AN 95:30482 SCISEARCH
- L25 ANSWER 25 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Stabilization of protein drug (catalase) by crosslinking to human serum albumin with polyethylene glycol
- SO (1993) 150 pp. Avail.: Univ. Microfilms Int., Order No. DA9511739 From: Diss. Abstr. Int. B 1995, 55(12) 5355
- AU Lo, Shi-Lung
- AN 1995:668067 HCAPLUS
- DN 123:93022
- L25 ANSWER 26 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Enzyme electrode with redox enzyme and polymer with multiple redox centers
- SO U.S., 15 pp. CODEN: USXXAM
- IN Gregg, Brian A.; Heller, Adam
- AN 1994:129005 HCAPLUS
- DN 120:129005

	PATENT NO.					KIND DATE				I	APPI	LICAT		DATE				
ΡI	US	5262	035			A	-	1993	 1116	Ţ	JS :	 1989-:	3892	26		19	9890	802
	US	5264	104			A		1993	1123	Į	JS 3	1992-	8807	50		1	9920	508
	US	5264	105			Α		1993	1123	τ	JS :	1993-	3280	5		15	9930	317
	WO	9323	744			A1		1993	1125	V	OV :	1993-1	US25	38		19	9930	319
		W:	AT,	AU,	BB,	BG,	BR,	CA,	ĊH,	DE,	DK,	, ES,	FI,	GB,	HU,	JP,	ΚP,	KR,
												, RU,						
		RW:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IE,	ΙT,	LU,	MC,	NL,	PT,	SE,
			BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	ML	, MR,	SN,	TD,	TG			
	AU	9339	274			A1		1993	1213	I	UA	1993	3927	4		19	9930	319
	ΕP	6392	68			<b>A</b> 1		1995	0222	E	EP :	1993-	9084	58	•	15	9930	319
		R:	DE,	DK,	FR,	GB,	IT											•
	JΡ	0750	6674		-	T2		1995	0720	٠	JP :	1993-	5201	91		15	9930	319

- L25 ANSWER 27 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Capillary column
- SO Jpn. Kokai Tokkyo Koho, 8 pp. CODEN: JKXXAF
- IN Mizuno, Masako; Tochigi, Kenji
- AN 1994:338112 HCAPLUS
- DN 120:338112

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PΙ	JP 05288716	A2	19931102	JP 1992-88909	19920409

- L25 ANSWER 28 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Protein crosslinking reagents cleavable within acidified intracellular vesicles
- SO U. S. Pat. Appl., 54 pp. Avail. NTIS Order No. PAT-APPL-6-204 163. CODEN: XAXXAV
- IN Neville, D. M.; Srinivasachar, K.

AN DN	1990:112047 112:112047 PATENT NO.	HCAPLUS KIND	DATE	APPLICATION NO.	DATE
PI .	US 204163	A0	19890315	US 1988-204163	19880601
	US 5066490 WO 8911867 W: AU,	A A1		WO 1989-US2349	19890531
		BE, CH, DE, 1 A1 B2	19900105		. 19890531
	EP 417188	A1	19910320	EP 1989-906910	19890531
	R: AT, I JP 03502098			I, LU, NL, SE JP 1989-506589	19890531
L25 TI	Cross-linking			005 ACS on STN ng bis-O-tosylates o	f diols, glycols,
so	165-8		-	ences (1988), 542(En	zyme Eng. 9),
AU AN DN	CODEN: ANYAA! Sundaram, P. 1989:453247 111:53247	V.	7-8923		
L25 TI	Immobilized	lipases in o	organic solve	C 2005 THE THOMSON CO ents; resterification (conf	
SO AU AN	World Conf.	Biotechnol.Fa awamoto T; Ka	ats + Oils Ir	id.; (1988) 123-30 to T; Sonomoto K	ozonec papez,
L25 TI	Effect of po	lyethylene g	lycol on the	2005 ACS on STN photochemical immobi	lization of an
so	enzyme in pho Makromolekula CODEN: MACEAN	are Chemie (	1987), 188(4)		
AU AN DN	Ichimura, Ku 1987:191795 106:191795	nihiro			
L25 TI	Fixing enzyme crosslinking	e by gel-inc	lusion proces		on STN
ΡI	acrylate. JP 60168386 JP 03069511		331 (198541), 101 (199148)	4	
=> d	ab 14,23,28				

MEDLINE on STN DUPLICATE 1 L25 ANSWER 14 OF 32 The explosion in commercial and synthetic applications of enzymes has AB stimulated much of the interest in enhancing enzyme functionality and stability. Covalent chemical modification, the original method available for altering protein properties, has now re-emerged as a powerful complementary approach to site-directed mutagenesis and directed evolution for tailoring proteins and enzymes. Glutaraldehyde crosslinking of enzyme crystals and polyethylene glycol (PEG) modification of enzyme surface amino groups are practical. methods to enhance biocatalyst stability. Whereas crosslinking of enzyme crystals generates easily recoverable insoluble biocatalysts, PEGylation increases solubility in organic solvents. Chemical modification has been exploited for the incorporation of cofactors onto protein templates and

for atom replacement in order to generate new functionality, such as the conversion of a hydrolase into a peroxidase. Despite the breadth of applicability of chemically modified enzymes, a difficulty that has previously impeded their implementation is the lack of chemo- or regio-specificity of chemical modifications, which can yield heterogeneous and irreproducible product mixtures. This challenge has recently been addressed by the introduction of a unique position for modification by a site-directed mutation that can subsequently be chemically modified to introduce an unnatural amino acid sidechain in a highly chemo- and regio-specific manner.

L25 ANSWER 23 OF 32 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN AB US 5324844 A UPAB: 19981104

A polyalkylene oxide having a mol.weight of less than 20,000, where at least one end qp. is an oxycarbonyl-oxy-N-dicarboximide qp.is new.

Pref. the polyalkylene oxide is of formula R1-(O-R2)a-(O-R3)q-(O-R4)c-O-CO-O-R5 in which, R1 = H, CH3, or a carbonyloxy N-dicarboxyimide gp. R2-R4 - alkyl; R5 = N-dicarboximide gp.; a = 1-1,000 and b, = 0-1,000.

USE - To effect covalent attachment of PEG to a protein, the OH end gps. are converted to reactive functional gps.. The most common form of activated PEG is poly(ethyleneglycol) succinoyl-N-hydroxy-succinimide (SS-PEG). This and the present cpds. each to chemically modify polypeptides to reduce immunogenicity and antigenicity and increase lifetime in the bloodstream as compared to the parent polypeptides. These beneficial properties of the modified polypeptides make them very useful in a variety of therapeutic applications, such as enzyme therapy. The reactivity of SC-PEG and BSC-PEG is comparable to that of SS-PEG. Thus high degrees of modification are available in mild conditions (aqueous buffer, pH 5.8-11, pref. 7.0-9.5) within 30-60 mins. and at moderate temps. (4-40 deg.C.). Also the new agents are soluble in a variety of organic solvents, thus being useful in the coupling of low mol.weight partially protected peptides and other biologically useful ligands. An additional advantage of succinimide carbonate activated PEG is that those activated functional qps. that do not react with amino qps. of a protein undergo fast aqueous hydrolysis producing non-toxic N-hydroxysuccinimide, CO2 and hydroxy-terminated PEG. This is of particular importance in the case of BSC-PEG which can serve a dual purpose, vis PEG-ylation and crosslinking. Biological activities of proteins modified with the new cpds. are preserved to a large extent. Dwg.0/3

L25 ANSWER 28 OF 32 HCAPLUS COPYRIGHT 2005 ACS on STN AB A biol. active substance (e.g. a cytotoxin, other drug, protein, enzyme, or nucleic acid) is delivered to cells (e.g. by receptor-mediated endocytosis) as a conjugate (e.g. an immunotoxin or prodrug) which can be cleaved within the cells under acidic conditions (e.g. at pH 5.4 in vesicles). The bifunctional crosslinking agent used in preparation of the conjugate is a ketal I [A = bridge unit, preferably (CH2)n; n = 1-8; R =C1-9 alkyl (preferably Me), (substituted) Ph], an acetal II [A as defined above; B = A, C6H4(CH2)n], or an ortho ester III (A as above). These crosslinking agents can also be used to couple proteins reversibly to matrixes for synthetic and chromatog. purposes. Thus, I (A = CH2CH2) (IV) was prepared by ketal exchange between N-(2-hydroxyethyl)maleimide and 2,2-dimethoxypropane. A nicked diphtheria toxin monomer was thiolated with iminothiolane and crosslinked to human T-cell surface antigen CD5 with IV. The toxicity of this conjugate toward target Jurkat cells was 50-fold greater than that of a similar conjugate prepared with a noncleavable crosslinker, bis(maleimidohexane).

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730058 ENZYME#
             1 L1 (5A) LINKER? (5A) (PROTEIN# OR ENZYME#)
L26
FILE 'SCISEARCH'
         12657 LINKER?
       1400079 PROTEIN#
        459972 ENZYME#
L27
             6 L2 (5A) LINKER? (5A) (PROTEIN# OR ENZYME#)
FILE 'LIFESCI'
         4489 LINKER?
        522211 PROTEIN#
        197816 ENZYME#
L28
             0 L3 (5A)LINKER?(5A)(PROTEIN# OR ENZYME#)
FILE 'BIOTECHDS'
          4471 LINKER?
        136948 PROTEIN#
        122684 ENZYME#
             2 L4 (5A) LINKER? (5A) (PROTEIN# OR ENZYME#)
L29
FILE 'BIOSIS'
        10838 LINKER?
       1669165 PROTEIN#
        772072 ENZYME#
             2 L5 (5A)LINKER?(5A)(PROTEIN# OR ENZYME#)
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FILE 'EMBASE'
          9200 LINKER?
       1410253 PROTEIN#
        787204 ENZYME#
             0 L6 (5A)LINKER?(5A)(PROTEIN# OR ENZYME#)
L31
FILE 'HCAPLUS'
        19537 LINKER?
       2014283 PROTEIN#
        929021 ENZYME#
            10 L7 (5A) LINKER? (5A) (PROTEIN# OR ENZYME#)
L32
FILE 'NTIS'
           176 LINKER?
         18093 PROTEIN#
         12052 ENZYME#
             0 L8 (5A)LINKER? (5A) (PROTEIN# OR ENZYME#)
L33
FILE 'ESBIOBASE'
         6032 LINKER?
        655527 PROTEIN#
        226276 ENZYME#
L34
             2 L9 (5A)LINKER?(5A)(PROTEIN# OR ENZYME#)
FILE 'BIOTECHNO'
         5399 LINKER?
        653195 PROTEIN#
        353854 ENZYME#
L35
             0 L10(5A)LINKER?(5A)(PROTEIN# OR ENZYME#)
FILE 'WPIDS'
          7635 LINKER?
        142087 PROTEIN#
         78914 ENZYME#
             4 L11(5A)LINKER?(5A)(PROTEIN# OR ENZYME#)
L36
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TOTAL FOR ALL FILES

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=> dup rem 137
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PROCESSING COMPLETED FOR L37

L38 22 DUP REM L37 (5 DUPLICATES REMOVED)

=> d tot

- L38 ANSWER 1 OF 22 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
- TI Construction of PEGylated gold colloid-assembled surface for high performance biosensor
- KOBUNSHI RONBUNSHU, (FEB 2005) Vol. 62, No. 2, pp. 81-86.
  Publisher: SOC POLYMER SCIENCE JAPAN, TSUKIJI DAISAN NAGAOKA BLDG, 2-4-2
  TSUKIJI, CHUO-KU, TOKYO, 104, JAPAN.
  ISSN: 0386-2186.
- AU Ishii T (Reprint); Suzuki Y; Akiyama Y; Otsuka H; Kataoka K; Nagasaki Y
- AN 2005:279872 SCISEARCH
- L38 ANSWER 2 OF 22 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
- TI Use of a Ble fusion protein as an expression and folding marker, as an affinity tag or as an expression and folding marker and an affinity tag, particularly, as markers for protein expression and/or folding; recombinant bleomycin fusion protein production and DNA microarray for
  - use in protein expression analysis
    HART D; GODBER B; BLACKBURN J M; MCANDREWS M
- AN 2004-15542 BIOTECHDS
- PI WO 2004046730 3 Jun 2004
- L38 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI PEG-physiologically active polypeptide homodimer complex having prolonged in vivo half-life and process for the preparation thereof
- SO PCT Int. Appl., 26 pp.

CODEN: PIXXD2

- IN Kim, Young Min; Kim, Dae Jin; Bae, Sung Min; Lim, Chang Ki; Kim, Kyeong Bae; Kwon, Se Chang; Lee, Gwan Sun
- AN 2004:857621 HCAPLUS
- DN 141:337646

PATENT NO. KIND DATE APPLICATION OF THE PROPERTY OF THE PROPER	
PT WO 2004087739 A1 20041014 WO 2004-F	
PT WO 2004087739 A1 20041014 WO 2004-1	KR781 20040403
11 110 2001007,35 AT 20041014 NO 2004 I	
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG,	BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC,	EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,	KE, KG, KP, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN,	MW, MX, MZ, NA, NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,	SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,	VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ,	TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG,	CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,	NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,	GQ, GW, ML, MR, NE, SN,
TD, TG	

- L38 ANSWER 4 OF 22 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Novel bispecific molecule comprising a first recognition binding moiety that binds C3b-like receptor, cross-linked through a polyethylene glycol linker to second recognition binding moieties that bind molecules other than C3b-like receptors.
- PI WO 2004024889 A2 20040325 (200431)\* EN 95 C12N000-00
  - RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
  - W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH

PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

AU 2003270686 A1 20040430 (200462) C12N000-00 IN CASEY, L; LEE, L S; MOHAMED, N; PORTER, J P; SESAY, M; WANG, X

L38 ANSWER 5 OF 22 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

Producing activated ester of polyethylene glycol (PEG) useful for PEGylation of biologically active peptides and proteins, by activating PEG with N,N'-disuccinimidyl oxalate or 1,1'-bis(6-(trifluoromethyl)benzotriazolyl) oxalate.

PI US 2004162388 A1 20040819 (200460) \* 13 C07K014-47 WO 2004074345 A2 20040902 (200460) EN C08G065-00

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

IN TJOENG, F S

L38 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN

TI Use of P97 as an enzyme delivery system for the delivery of therapeutic lysosomal enzymes

SO PCT Int. Appl., 48 pp. CODEN: PIXXD2

IN Starr, Christopher M.; Zankel, Todd

AN 2003:551350 HCAPLUS

DN 139:106432

211	PATENT NO.				KIND DATE				APPLICATION NO.						DATE		
						-											
ΡI	WO 2003	05717	79		A2 20030717			1	WO 2	003-1	JS89	4		20	0030	110	
	WO 2003	05717	79		<b>A</b> 3		2003	1204									
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DΖ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
		PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,
		UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW						
	RW:	GH,	GM,	KΕ,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
		KG,	ΚZ,	MD,	RU,	TJ,	TM,	AT,	ΒE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	ΝL,	PT,	SE,	SI,	SK,	TR,	BF,
		ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG	
	EP 1463512				A2		2004	1006	;	EP 2	003-	7178	70		20	0030	1'10
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK	

- L38 ANSWER 7 OF 22 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
- TI Surface modification of a novel porous titanium dioxide/glass composite
- SO MATERIALWISSENSCHAFT UND WERKSTOFFTECHNIK, (DEC 2003) Vol. 34, No. 12, pp. 1058-1063.

Publisher: WILEY-V C H VERLAG GMBH, PO BOX 10 11 61, D-69451 WEINHEIM, GERMANY.

ISSN: 0933-5137.

AU Erli H J (Reprint); von Walter M; Ragoss C; Steffens G C M; Paar O; Maier H R

AN 2004:127666 SCISEARCH

L38 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN

TI PEG pro-linkers: Applications to biologically active molecules and proteins

SO Polymeric Materials Science and Engineering (2003), 89, 627 CODEN: PMSEDG; ISSN: 1550-6703

- Greenwald, Richard B.; Grau, Uli; Choe, Yun H.; Zhao, Hong ΑIJ
- 2003:666858 HCAPLUS ΑN
- 140:169494 DN
- ANSWER 9 OF 22 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on L38
- ΤI Val-ala-pro-gly, an elastin-derived non-integrin ligand: Smooth muscle cell adhesion and specificity
- JOURNAL OF BIOMEDICAL MATERIALS RESEARCH PART A, (1 OCT 2003) Vol. 67A, SO No. 1, pp. 255-259.

Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012 USA.

ISSN: 0021-9304.

- Gobin A S; West J L (Reprint) ΑU
- AN2003:889096 SCISEARCH
- L38 ANSWER 10 OF 22 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
- TI New immunoglobulin (Ig)G monoclonal antibody, useful for detection of a target, and purification of a target e.g. peptides, proteins, enzymes, cytokines, hematopoietins, growth factors, and hormones;

monoclonal antibody and humanized antibody production useful for protein purification, DNA purification, RNA purification and diagnosis

- ΑU ROBERTS M J; GREEN M E
- 2003-09031 BIOTECHDS AN
- PΙ WO 2002094853 28 Nov 2002
- ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN L38
- Use of human receptor activator of NF-κB and osteoprotegerin variants with improved ligand binding activity for treatment of osteoporosis and bone disorders
- PCT Int. Appl., 129 pp. SO
  - CODEN: PIXXD2
- Haaning, Jesper Mortensen; Halkier, Torben IN
- AN2002:637829 HCAPLUS

DN	137:181397 PATENT NO.			KIND DATE			APPLICATION NO.						DATE			
ΡI	WO 200	2064782		A2 20020822			1	WO 2	002-1	DK90			2	0020	208	
	WO 2002	2064782		A3		2004	0108									
	W :	AE, A	G, AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		CO, C	R, CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM, H	R, HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,
		LS, L	r, LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
		PL, P	r, RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TN,	TR,	TT,	TZ,
		UA, U	G, US,	UZ,	VN,	YU,	ZA,	ZM,	ZW							
	RW	GH, G	M, KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
			Z, MD,	-								-				
		GR, I	E, IT,	LU,	MC,	ΝL,	PT,	SE,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,
		GN, G	Q, GW,	ML,	MR,	ΝE,	SN,	TD,	TG							
	EP 1399	P 1399555		A2		2004	0324	:	EP 2	002-	7117	78		2	00202	208
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	US 2004	132971		A1		2004	0708	1	US 2	004-	4672	43		2	0040	112

- L38 ANSWER 12 OF 22 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- ΤI Evaluating solid phase for use in dual bead assay, involves binding solid phase to probe optionally in presence of cross-linking agent and determining amount of probe bound covalently to solid phase.
- PΙ WO 2002068696 A2 20020906 (200315) \* EN 137 C12Q001-68
  - RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
  - W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT

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RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
    US 2002168663
                   A1 20021114 (200315)
                                                    C12Q001-68
                    A1 20030424 (200330)
                                                    C12Q001-68
    US 2003077598
                    A1 20020912 (200433)
                                                    C12Q001-68
    AU 2002238142
    LAM, A H; PHAN, B C; VIRTANEN, J A; YEUNG, K
IN
L38 ANSWER 13 OF 22 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
    Macromolecular solid particles for transporting hydrophobic active agents
    e.g. drugs or nucleic acids, comprise molecular backbone, polycondensate
    side chains and side chain terminals having free reactive groups.
                   A2 20020103 (200230)* GE 134
    WO 2002000191
                                                  A61K009-00
ΡI
       RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
           NL OA PT SD SE SL SZ TR TZ UG ZW
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           KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
           SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
    AU 2001081921
                   A 20020108 (200235)
                                                    A61K009-00
    EP 1333806
                    A2 20030813 (200355) GE
                                                    A61K009-00
        R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
           RO SE SI TR
    US 2004062815
                   A1 20040401 (200424)
                                                    A61K009-16
    FLAIG, R M; FRICKER, G
IN
L38 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ΤI
    Substrate Specificity of the Integral Membrane Protease OmpT Determined by
    Spatially Addressed Peptide Libraries
SO
    Biochemistry (2001), 40(6), 1694-1701
    CODEN: BICHAW; ISSN: 0006-2960
    Dekker, Niek; Cox, Ruud C.; Kramer, R. Arjen; Egmond, Maarten R.
ΑU
    2001:36316 HCAPLUS
AN
    134:233492
DN
L38
    ANSWER 15 OF 22
                        MEDLINE on STN
                                                       DUPLICATE 1
    Drug delivery systems employing 1,6-elimination: releasable poly(ethylene
    glycol) conjugates of proteins.
    Bioconjugate chemistry, (2001 Mar-Apr) 12 (2) 163-9.
SO
    Journal code: 9010319. ISSN: 1043-1802.
    Lee S; Greenwald R B; McGuire J; Yang K; Shi C
ΑU
    2001459730
                 MEDLINE
AN
    ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
L38
TI
    Laundry detergent and/or fabric care compositions comprising an enzyme
    modified with a cellulose-binding domain
     PCT Int. Appl., 96 pp.
SO
    CODEN: PIXXD2
    Smets, Johan; Bettiol, Jean-Luc Philippe; Boyer, Stanton Lane; Busch,
IN
    Alfred
    1999:723153 HCAPLUS
AN
DN
    131:324165
    PATENT NO.
                       KIND
                               DATE
                                          APPLICATION NO.
                                                                 DATE
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                               -----
                                          _____
                        A1 19991111 WO 1998-US8856
    WO 9957250
                                                                 19980501
        W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
            KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
            NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
           -UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
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            CM, GA, GN, ML, MR, NE, SN, TD, TG
                              19991123
                                           AU 1998-72754
                                                                  19980501
    AU 9872754
                        A1
                                           CA 1999-2330614
                        AA
                               19991111
                                                                  19990430
    CA 2330614
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A1

WO 9957252

19991111

WO 1999-US9453

19990430

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W: BR, CA, CN, IN, JP, MX, US
          RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
              PT, SE
                                   20010109
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     BR 9910151
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                                   20010109
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     EP 1073724
                            A1
                                   20010207
                                                EP 1999-920204
                                                                          19990430
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                            T2
                                   20030729
                                                JP 2000-547208
                                                                          19990430
     JP 2003522517
     US 6465410
                            B1
                                   20021015
                                                US 2000-674471
                                                                          20001101
     US 6468955
                            В1
                                   20021022
                                                US 2000-674478
                                                                          20001101
    ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
L38
     Activated PEG linkers and methods for making and purifying them
TI
SO
     PCT Int. Appl., 56 pp.
     CODEN: PIXXD2
IN
     Ibrahim, Prabha N.; Baile, Robert A.; Seely, James Ervin
     1997:617995 HCAPLUS
AN
DN
     127:268033
     PATENT NO.
                           KIND
                                   DATE
                                                APPLICATION NO.
                           ----
     WO 9732607
                                   19970912
                                                WO 1996-US19459
                                                                          19961206
ΡÍ
                            A2
     WO 9732607
                            Α3
                                   19971113
          W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
              AL, AM, AI, AO, AZ, BA, BB, BG, BK, BI, CA, CH, CN, CO, CZ, BE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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              IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
              MR, NE, SN, TD, TG
                                   19980505
                                                US 1996-611918
                                                                          19960306
     US 5747639
                            Α
                            AA
                                   19970912
                                                CA 1996-2248006
                                                                          19961206
     CA 2248006
     CA 2248006
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                                   20020528
     AU 9714108
                            A1
                                   19970922
                                                AU 1997-14108
                                                                          19961206
     AU 720399
                            B2
                                   20000601
                                                EP 1996-944251
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     EP 906122
                            A2
                                   19990407
     EP 906122
                                   20030910
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              IE, SI, LT, LV, FI, RO
                            T2
                                                JP 1997-531747
                                   20000606
                                                                          19961206
     JP 2000506851
     AT 249244
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                            E
                                   20030915
     PT 906122
                            Т
                                                PT 1996-944251
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                                   20031231
     ES 2206616
                            Т3
                                   20040516
                                                ES 1996-944251
                                                                          19961206
     US 5935564
                            Α
                                   19990810
                                                US 1997-936478
                                                                          19970918
L38 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
ΤI
     Issues encountered in the production of site-specific mono-PEGylated
     therapeutic proteins
     Polymer Preprints (American Chemical Society, Division of Polymer
SO
     Chemistry) (1997), 38(1), 572-573
     CODEN: ACPPAY; ISSN: 0032-3934
ΑU
     Seely, Jim; Richey, Carl; Grasel, Tim; Wilson, John
ΑN
     1997:224409 HCAPLUS
DN
     126:268347
     ANSWER 19 OF 22 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on
L38
                                                              DUPLICATE 2
TI
     PEG thiazolidine-2-thione, a novel reagent for facile protein
     modification: Conjugation of bovine hemoglobin
SO
     BIOCONJUGATE CHEMISTRY, (NOV-DEC 1996) Vol. 7, No. 6, pp. 638-641.
     Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
     ISSN: 1043-1802.
     Greenwald R B (Reprint); Pendri A; Martinez A; Gilbert C; Bradley P
ΑU
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96:896460 SCISEARCH

AN

- L38 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Poly(ethylene glycol) Fluorescent Linkers
- SO Bioconjugate Chemistry (1995), 6(5), 596-8 CODEN: BCCHES; ISSN: 1043-1802
- AU Pendri, Annapurna; Martinez, Anthony; Xia, Jing; Shorr, Robert G. L.; Greenwald, Richard B.
- AN 1995:790826 HCAPLUS
- DN 123:229223
- L38 ANSWER 21 OF 22 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
- TI MANUFACTURING OF RECOMBINANT TUMOR-NECROSIS-FACTOR BINDING-PROTEIN DUMBBELL USING A 20K PEG BIS-VINYLSULFONE LINKER
- SO ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, (02 APR 1995) Vol. 209, Part 1, pp. 68-BIOT. ISSN: 0065-7727.
- AU SEELY J (Reprint); RICHEY C; TODD B
- AN 95:623781 SCISEARCH
- L38 ANSWER 22 OF 22 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
- TI Manufacturing of recombinant tumor necrosis factor binding protein "dumbbell" using a 20K PEG bis-vinylsulfone linker.
- SO Abstracts of Papers American Chemical Society, (1995) Vol. 209, No. 1-2, pp. BIOT 68.

  Meeting Info.: 209th American Chemical Society National Meeting. Anaheim, California, USA. April 2-6, 1995.

  CODEN: ACSRAL. ISSN: 0065-7727.
- AU Seely J., C. Richey; Todd, B.
- AN 1995:239228 BIOSIS

## => d ab 17,19,20

- L38 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
- AB Activated PEG linkers, particularly those having reactive Michael acceptors, are prepared which can be used to modify biol. active mols. and improve overall production of such mols. An efficient process is provided for purifying the activated linkers by hydrophobic interaction chromatog. (HIC) to sep. the activated linkers based on their size and on their end-group functionality. Thus, PEG (20 kDa) reacted with divinyl sulfone to form PEG bis(vinyl sulfone) (I). I bound completely to ToyoPearl Bu 650C resin in the presence of 1.75M NaCl or 0.25M Na2SO4; elution with a linear NaCl gradient separated 20-kDa I from high-mol.-weight I. The 20-kDa I was conjugated with a reduced tumor necrosis factor-binding protein mutein, and products bearing tumor necrosis factor at one or both ends of PEG were separated by HIC on ToyoPearl Bu 650C.
- L38 ANSWER 19 OF 22 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 2
- AB A novel PEG linker that employs a thiazolidine-2-thione group has been synthesized. Kinetic studies done on this compound demonstrate a relatively long half-life compared to those of traditional succinimidyl linkers. This new PEG derivative reacts with proteins under mild conditions and was utilized to conjugate bovine hemoglobin (bHb) to provide a PEG amide-linked protein. The physical characteristics of this conjugate were compared with those of the known PEG carbamate-linked bHb.
- L38 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2005 ACS on STN
- AB The first examples of PEG linkers containing the highly fluorescent dansyl group were synthesized. Quantum yields of these PEG fluorescent linker were determined and utilized in calculating the PEG number of various protein

conjugates. The method was also shown to be applicable to lower mol. weight drugs as exemplified by taxol.

=> log y

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 150.82 151.03

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION

CA SUBSCRIBER PRICE -2.19 -2.19

STN INTERNATIONAL LOGOFF AT 08:27:24 ON 20 APR 2005

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COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 0.21 0.21

FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS, ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 08:39:26 ON 20 APR 2005 ALL COPYRIGHTS AND RESTRICTIONS APPLY. SEE HELP USAGETERMS FOR DETAILS.

11 FILES IN THE FILE LIST

=> s protein#(5a)conjugat?

FILE 'MEDLINE'

1759365 PROTEIN#

75574 CONJUGAT?

L1 5319 PROTEIN#(5A) CONJUGAT?

FILE 'SCISEARCH'

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106571 CONJUGAT?

L2 4883 PROTEIN#(5A)CONJUGAT?

FILE 'LIFESCI'

522211 PROTEIN#

22489 CONJUGAT?

L3 2177 PROTEIN# (5A) CONJUGAT?

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136948 PROTEIN#

8285 CONJUGAT?

L4 973 PROTEIN#(5A)CONJUGAT?

FILE 'BIOSIS'

1669165 PROTEIN#

84018 CONJUGAT?

L5 6274 PROTEIN#(5A) CONJUGAT?

FILE 'EMBASE'

1410253 PROTEIN#

72830 CONJUGAT?

L6 4612 PROTEIN#(5A) CONJUGAT?

FILE 'HCAPLUS'

2014283 PROTEIN#

207032 CONJUGAT?

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13409 PROTEIN# (5A) CONJUGAT?
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           208 PROTEIN# (5A) CONJUGAT?
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FILE 'BIOTECHNO'
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=> s (peg or polyethylene glycol)(10a)link?
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          8959 PEG
         33678 POLYETHYLENE
         22000 GLYCOL
          9086 POLYETHYLENE GLYCOL
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        382837 LINK?
           309 (PEG OR POLYETHYLENE GLYCOL) (10A) LINK?
FILE 'SCISEARCH'
         14973 PEG
         49789 POLYETHYLENE
         36174 GLYCOL
         11455 POLYETHYLENE GLYCOL
                  (POLYETHYLENE (W) GLYCOL)
        411725 LINK?
           519 (PEG OR POLYETHYLENE GLYCOL) (10A) LINK?
FILE 'LIFESCI'
          2228 PEG
          4480 "POLYETHYLENE"
          5906 "GLYCOL"
          3000 POLYETHYLENE GLYCOL
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        128013 LINK?
            85 (PEG OR POLYETHYLENE GLYCOL) (10A) LINK?
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FILE 'BIOTECHDS'

L7

L8

L9

L10

L11

L12

L13

L14

L15

6044 PEG

3945 POLYETHYLENE

4515 GLYCOL

3036 POLYETHYLENE GLYCOL

(POLYETHYLENE (W) GLYCOL)

30772 LINK?

L16 127 (PEG OR POLYETHYLENE GLYCOL) (10A) LINK?

FILE 'BIOSIS'

11854 PEG

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23925 POLYETHYLENE
         32559 GLYCOL
         14532 POLYETHYLENE GLYCOL
                  (POLYETHYLENE (W) GLYCOL)
        340098 LINK?
           327 (PEG OR POLYETHYLENE GLYCOL) (10A) LINK?
L17
FILE 'EMBASE'
          8915 PEG
         18670 "POLYETHYLENE"
         28246 "GLYCOL"
          8533 POLYETHYLENE GLYCOL
                  ("POLYETHYLENE" (W) "GLYCOL")
        339891 LINK?
           325 (PEG OR POLYETHYLENE GLYCOL) (10A) LINK?
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FILE 'HCAPLUS'
         31703 PEG
        323028 POLYETHYLENE
        328789 GLYCOL
         90639 POLYETHYLENE GLYCOL
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        418245 LINK?
L19
          1011 (PEG OR POLYETHYLENE GLYCOL) (10A) LINK?
FILE 'NTIS'
           321 PEG
          5591 POLYETHYLENE
          1894 GLYCOL
           253 POLYETHYLENE GLYCOL
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         32483 LINK?
            12 (PEG OR POLYETHYLENE GLYCOL) (10A) LINK?
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FILE 'ESBIOBASE'
          3672 PEG
          4796 POLYETHYLENE
          6391 GLYCOL
          3005 POLYETHYLENE GLYCOL
                  (POLYETHYLENE (W) GLYCOL)
        144684 LINK?
L21
           174 (PEG OR POLYETHYLENE GLYCOL) (10A) LINK?
FILE 'BIOTECHNO'
          2816 PEG
          4665 POLYETHYLENE
          7260 GLYCOL
          3167 POLYETHYLENE GLYCOL
                  (POLYETHYLENE (W) GLYCOL)
        173624 LINK?
           170 (PEG OR POLYETHYLENE GLYCOL) (10A) LINK?
L22
FILE 'WPIDS'
         15802 PEG
        197943 POLYETHYLENE
        109036 GLYCOL
         26705 POLYETHYLENE GLYCOL
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        444068 LINK?
L23
           772 (PEG OR POLYETHYLENE GLYCOL) (10A) LINK?
TOTAL FOR ALL FILES
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3831 (PEG OR POLYETHYLENE GLYCOL) (10A) LINK?

L24

=> s 112 and 124

FILE 'MEDLINE'

L25 12 L1 AND L13

FILE 'SCISEARCH'

L26 16 L2 AND L14

FILE 'LIFESCI'

L27 2 L3 AND L15

FILE 'BIOTECHDS'

L28 6 L4 AND L16

FILE 'BIOSIS'

L29 13 L5 AND L17

FILE 'EMBASE'

L30 9 L6 AND L18

FILE 'HCAPLUS'

L31 63 L7 AND L19

FILE 'NTIS'

L32 0 L8 AND L20

FILE 'ESBIOBASE'

L33 8 L9 AND L21

FILE 'BIOTECHNO'

L34 0 L10 AND L22

FILE 'WPIDS'

L35 19 L11 AND L23

TOTAL FOR ALL FILES

L36 148 L12 AND L24

=> s 136 not 1999-2005/py

FILE 'MEDLINE'

3325502 1999-2005/PY

L37 4 L25 NOT 1999-2005/PY

FILE 'SCISEARCH'

6385167 1999-2005/PY

L38 8 L26 NOT 1999-2005/PY

FILE 'LIFESCI'

647543 1999-2005/PY

L39 1 L27 NOT 1999-2005/PY

FILE 'BIOTECHDS'

126993 1999-2005/PY

L40 0 L28 NOT 1999-2005/PY

FILE 'BIOSIS'

3277108 1999-2005/PY

L41 4 L29 NOT 1999-2005/PY

FILE 'EMBASE'

2914482 1999-2005/PY

L42 3 L30 NOT 1999-2005/PY

FILE 'HCAPLUS'

6178020 1999-2005/PY

FILE 'NTIS'

108997 1999-2005/PY

L44 0 L32 NOT 1999-2005/PY

FILE 'ESBIOBASE'

1817014 1999-2005/PY

L45 3 L33 NOT 1999-2005/PY

FILE 'BIOTECHNO'

611346 1999-2005/PY

L46 0 L34 NOT 1999-2005/PY

FILE 'WPIDS'

5325720 1999-2005/PY

L47 3 L35 NOT 1999-2005/PY

TOTAL FOR ALL FILES

L48 41 L36 NOT 1999-2005/PY

=> dup rem 148

PROCESSING COMPLETED FOR L48

L49 20 DUP REM L48 (21 DUPLICATES REMOVED)

=> d tot

L49 ANSWER 1 OF 20 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
TI Detecting/treating target cells, tissues or pathogens - by a

pre-targetting method which uses improved chelate conjugates, which can improve the amount of radionuclide delivered to the target.

PI WO 9804293 A1 19980205 (199813) \* EN 38 A61K051-00

RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 9740474 A 19980220 (199828) A61K051-00

IN GRIFFITHS, G L; HANSEN, H J; KARACAY, H

- L49 ANSWER 2 OF 20 MEDLINE on STN DUPLICATE 1
- TI Short communication: renal tubular vacuolation in animals treated with polyethylene-glycol-conjugated proteins.
- SO Toxicological sciences: an official journal of the Society of Toxicology, (1998 Apr) 42 (2) 152-7.

  Journal code: 9805461. ISSN: 1096-6080.
- AU Bendele A; Seely J; Richey C; Sennello G; Shopp G

AN 1998240182 MEDLINE

- L49 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN-
- TI Issues encountered in the production of site-specific mono-PEGylated therapeutic proteins
- SO Polymer Preprints (American Chemical Society, Division of Polymer Chemistry) (1997), 38(1), 572-573
  CODEN: ACPPAY; ISSN: 0032-3934
- AU Seely, Jim; Richey, Carl; Grasel, Tim; Wilson, John
- AN 1997:224409 HCAPLUS
- DN 126:268347
- L49 ANSWER 4 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 2
- TI Hydrazide derivatives of poly(ethylene glycol) and their bioconjugates
- SO ACS SYMPOSIUM SERIES, (FEB 1997) Vol. 680, pp. 318-341.

- Publisher: AMER CHEMICAL SOC, 1155 SIXTEENTH ST NW, WASHINGTON, DC 20036. ISSN: 0097-6156.
- AU Zalipsky S (Reprint); MenonRudolph S
- AN 1998:12679 SCISEARCH
- L49 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Novel degradable PEG esters for drug delivery: Synthesis and characterization.
- SO Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (1997), POLY-024 Publisher: American Chemical Society, Washington, D. C. CODEN: 64AOAA
- AU Zhao, Xuan; Harris, J. Milton
- AN 1997:163952 HCAPLUS
- L49 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
- TI Pegylated modified proteins
- SO PCT Int. Appl., 71 pp.

CODEN: PIXXD2

- IN Bona, Constantin; Brumeanu, Teodor-Doru
- AN 1997:97355 HCAPLUS
- DN 126:103109

	PATENT NO.	KIND DATE	APPLICATION NO.	DATE
PI	WO 9640731	A1 19961219	WO 1996-US8995	19960606
		DE, DK, ES, FI,	FR, GB, GR, IE, IT, LU,	
	AU 9662550	A1 19961230	AU 1996-62550	19960606

- L49 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Low diol polyalkylene oxide for modifying proteins to increase their half-life and reduce immunogenicity
- SO U.S., 36 pp., Cont.-in-part of U.S. Ser. No. 936,416, abandoned. CODEN: USXXAM
- IN Snow, Robert A.; Ladd, David L.; Hoyer, Denton W.
- AN 1996:452743 HCAPLUS
- DN 125:136431

211	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
			<b>-</b>		<b></b>
ΡI	US 5532150	A	19960702	US 1994-245999	19940519
	CA 2101361	AA	19940228	CA 1993-2101361	19930727
	JP 06172201	A2	19940621	JP 1993-210302	19930825
	AU 9344885	A1	19940303	AU 1993-44885	19930826
	AU 675798	B2	19970220	· ·	
	HU 66755	A2	19941228	HU 1993-2440	19930827
	US 5661020	A	19970826	US 1996-632300	19960415

- L49 ANSWER 8 OF 20 MEDLINE on STN DUPLICATE 4
- TI PEG thiazolidine-2-thione, a novel reagent for facile **protein** modification: **conjugation** of bovine hemoglobin.
- SO Bioconjugate chemistry, (1996 Nov-Dec) 7 (6) 638-41. Journal code: 9010319. ISSN: 1043-1802.
- AU Greenwald R B; Pendri A; Martinez A; Gilbert C; Bradley P
- AN 97107756 MEDLINE
- L49 ANSWER 9 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
- TI PROLONGED CIRCULATION OF RECOMBINANT HUMAN GRANULOCYTE-COLONY-STIMULATING FACTOR BY COVALENT LINKAGE TO ALBUMIN THROUGH A HETEROBIFUNCTIONAL POLYETHYLENE-GLYCOL
- SO PHARMACEUTICAL RESEARCH, (DEC 1995) Vol. 12, No. 12, pp. 1883-1888. ISSN: 0724-8741.
- AU PAIGE A G (Reprint); WHITCOMB K L; LIU J; KINSTLER O
- AN 96:69623 SCISEARCH

L49 ANSWER 10 OF 20 MEDLINE on STN DUPLICATE 5

- TI Poly(ethylene glycol) fluorescent linkers.
- SO Bioconjugate chemistry, (1995 Sep-Oct) 6 (5) 596-8. Journal code: 9010319. ISSN: 1043-1802.
- AU Pendri A; Martinez A; Xia J; Shorr R G; Greenwald R B
- AN 96113592 MEDLINE
- L49 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI PEG-protein constructs for clinical use
- Perspectives on Protein Engineering & Complementary Technologies,
  Collected Papers, International Symposium, 3rd, Oxford, Sept. 13-17, 1994
  (1995), Meeting Date 1994, 223-226. Editor(s): Geisow, Michael J.; Epton,
  Roger. Publisher: Mayflower Worldwide, Kingswinford, UK.
  CODEN: 62ZQAP
- AU Fisher, D.; Delgado, C.; Tejedor, M. C.; Malik, F.; Francis, G. E.
- AN 1996:398583 HCAPLUS
- DN 125:95896
- L49 ANSWER 12 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
- TI POLY(ETHYLENE GLYCOL)-MODIFIED PHOSPHOLIPIDS PREVENT AGGREGATION DURING COVALENT CONJUGATION OF PROTEINS TO LIPOSOMES
- SO BIOCONJUGATE CHEMISTRY, (MAR/APR 1995) Vol. 6, No. 2, pp. 187-194. ISSN: 1043-1802.
- AU HARASYM T O (Reprint); TARDI P; LONGMAN S A; ANSELL S M; BALLY M B; CULLIS P R; CHOI L S L
- AN 95:246092 SCISEARCH
- L49 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI **PEG** hydrazone and **PEG** oxime **linkage** forming reagents and protein derivatives.
- SO Eur. Pat. Appl., 47 pp. CODEN: EPXXDW
- IN Wright, David E.
- AN 1995:319762 HCAPLUS
- DN 122:89553

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ΡI	EP 605963	A2 19940713	EP 1993-309825	19931207
	EP 605963	A3 19951108		·
	R: AT, BE, CH,	DE, DK, ES, FR,	GB, GR, IE, IT, LI, LU	, MC, NL, PT, SE
	CA 2110543	AA 19940610	CA 1993-2110543	19931202
	FI 9305485	A 19940610	FI 1993-5485	19931208
	NO 9304477	A 19940610	NO 1993-4477	19931208
	ZA 9309214	A 19950608	ZA 1993-9214	19931208
	AU 9352383	A1 19940623	AU 1993-52383	19931209
	JP 07196925	A2 19950801	JP 1993-340709	19931209

- L49 ANSWER 14 OF 20 MEDLINE on STN DUPLICATE 6
- TI Quantitative analysis of polyethylene glycol (PEG) in PEG-modified proteins/cytokines by aqueous two-phase systems.
- SO Journal of biochemical and biophysical methods, (1994 Dec) 29 (3-4) 237-50.
  - Journal code: 7907378. ISSN: 0165-022X.
- AU Delgado C; Malik F; Selisko B; Fisher D; Francis G E
- AN 95213525 MEDLINE
- L49 ANSWER 15 OF 20 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New poly alkylene glycol aldehyde derivs. used to prepare antibody imine or amine conjugates.
- PI US 5252714 A 19931012 (199342)\* 5 C07K003-08
- IN HARRIS, J M; SEDAGHAT-HERATI, M R
- L49 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN

- TI A strategy for characterization of polyethylene glycol-derivatized proteins. A mass spectrometric analysis of the attachment sites in polyethylene glycol-derivatized superoxide dismutase
- SO Drug Metabolism and Disposition (1993), 21(5), 911-17 CODEN: DMDSAI; ISSN: 0090-9556
- AU Vestling, Martha M.; Murphy, Constance M.; Keller, Deborah A.; Fenselau, Catherine; Dedinas, Jonas; Ladd, David L.; Olsen, Mark A.
- AN 1994:86193 HCAPLUS
- DN 120:86193
- L49 ANSWER 17 OF 20 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
- TI Modification of **protein conjugated** drugs by polyethylene glycol.
- SO Current Opinion in Therapeutic Patents, (1993) Vol. 3, No. 1, pp. 93-94. ISSN: 0962-2594 CODEN: COTPES
- AN 93079714 EMBASE
- L49 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Hydrazine-containing conjugates of polypeptides and glycopolypeptides with polymers
- SO PCT Int. Appl., 39 pp. CODEN: PIXXD2
- IN Zalipsky, Samuel; Lee, Chyi; Menon-Rudolph, Sunitha
- AN 1993:76627 HCAPLUS
- DN 118:76627

	PATENT NO.				KIND DATE			APPLICATION NO.						DATE			
							-										
ΡI	WO	9216	555			<b>A</b> 1		1992	1001	WC	19	92 <b>-</b> t	JS20	47		1	9920312
		W:	AU,	CA,	HU,	JP,	KR	, RU									
		RW:	AT,	BE,	CH,	DE,	DK	, ES,	FR,	GB, G	R,	ΙT,	LU,	MC,	NL,	SE	
	AU	9216	769			A1		1992	1021	AU	J 19	92-3	1676	9		1	9920312
	EP	5765	89			A1		1994	0105	EF	19	92-9	9093	26		19	9920312
		R:	ΑT,	BE,	CH,	DE,	DK	, ES,	FR,	GB, G	R,	ΙT,	LI,	LU,	MC,	NL,	SE
	JP	0650	6217			T2		1994	0714	JF	19	92-5	5089	14		1:	9920312
	CA	2101	918			AA		1992	0919	CA	19	92-2	2101	918		1:	9920316

- L49 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Conjugates for targeted delivery of bone growth factors
- SO Eur. Pat. Appl., 9 pp. CODEN: EPXXDW
- IN Bentz, Hanne; Rosen, David
- AN 1993:66851 HCAPLUS
- DN 118:66851

	PA.		KINI	)	DATE A		APF	LICAT	'ION	NO.	DATE							
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ΡI	ΕP	5128	44			A1		1992	21111	1	EΡ	1992-	3041	42		19	9920	508
	EP	5128	44			B1		1997	70806									
		R:	AT,	BE,	CH,	DE,	DK	, ES,	FR,	GB,	GF	R, IT,	LI,	LU,	MC,	NL,	PT,	SE
	CA	2102	808			AA		1992	21111	(	CA	1992-	2102	808		19	920	507
	WO	9220	371			A1		1992	21126	1	OW	1992-	US38	40		19	9920	507
		W:	ΑU,	CA,	JP													
	AU	9219	947			A1		1992	21230	1	ΑU	1992-	1994	7		19	9920	507
	ΑU	6621	.55			B2		1995	0824									
	AT	1563	65			E		1997	70815	1	AΤ	1992-	3041	42		19	920	508
	ES	2104	827			Т3		1997	71016	]	ES	1992-	3041	42		19	920	508

- L49 ANSWER 20 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 7
- TI SUCCINIMIDYL CARBONATES OF POLYETHYLENE-GLYCOL USEFUL REACTIVE POLYMERS FOR PREPARATION OF **PROTEIN CONJUGATES**
- SO ACS SYMPOSIUM SERIES, (1991) Vol. 469, pp. 91-100.
- AU ZALIPSKY S (Reprint); SELTZER R; NHO K
- AN 91:505276 SCISEARCH

L49 ANSWER 1 OF 20 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN AB WO 9804293 A UPAB: 19980330

The following are claimed: (A) a method for detecting or treating target cells, tissues or pathogens ('the target material') in a patient, comprising: (a) pre-targeting the material with avidin, using a targeting protein that (i) specifically binds a marker substance on the target material, and to which (ii) avidin is bound either directly (as an avidin-targeting protein conjugate) or indirectly (via non-covalent bonding of avidin to a biotin-targeting protein conjugate); (b) parenterally injecting a detection or therapeutic composition (comprising a biotin-chelator conjugate and a chelatable metal ion detection/therapeutic agent), and allowing the composition to accrete at the target material, and (c) using the detection/therapeutic agent to detect or treat the target material. The chelate conjugate is (i) purified by chromatography after chelation of the metal ion, or (ii) also comprises a blood transit-modifying linker or addend which is covalently bound to the chelate conjugate, and (B) a sterile injectable composition, for human use, comprising: (a) a biotin-chelator conjugate and a chelatable metal ion detection/therapeutic agent; or (b) a biotin-chelator conjugate (to which a blood transit-modifying linker or addend is covalently bound) and a chelatable metal ion detection/therapeutic agent.

The chromatography is anion exchange chromatography. The blood transit-modifying linker or addend is dextran, polypeptide or polyethylene glycol. It has a fractional clearance by the kidney of < 1. It has an effective molecular radius of 15-40 Angstrom. The metal ion detection or therapeutic agent is an electron- or a neutron-capturing agent. The metal of the agent is antimony-119, actinium-225, rhenium-186, -188 or 189, silver-111, platinum-197, palladium-103 or 109, copper-67, etc. The chelating agent is DOTA (1,4,7,10-tetraazacyclododecane N,N',N'',N'''-tetraacetic acid). The multiple chelate conjugate is a metallothionein or comprises a synthetic polymer.

USE - The process may be used for detection and/or treatment of pathological conditions, such as tumours.

ADVANTAGE - Compared to prior art processes, the above processes allow delivery of higher amounts, higher specific activities and higher target:nontarget ratios of detection/therapeutic agents to target sites. They allow greater control of the residence time of administered detection and therapeutic agents in the body.

Dwg.0/0

ANSWER 2 OF 20 L49 MEDLINE on STN DUPLICATE 1 During toxicologic evaluation of a dimeric PEG-linked AB protein, tumor necrosis factor binding protein (TNF-bp), vacuolation of renal cortical tubular epithelium was seen in male and female Sprague-Dawley rats (200-300 g) given i.v. doses of 40, 20, or 10 mg/kg every other day for 3 months. Tubular lesions in rats treated with 20 or 40 mg/kg for 3 months were only partially reversible after a 2-month recovery period. Despite the presence of marked vacuolation, there were no changes in BUN, creatinine, urinalysis parameters, urinary NAG, urinary B2-microglobulin, or fractional sodium excretion. Single i.v. doses > or = 20 mg/kg TNF-bp caused similar but milder changes. However, equivalent doses of PEG alone or the non-PEG-linked TNF-bp did not cause light microscopic evidence of vacuolation. Treatment of rats with another **PEG-linked** protein of similar molecular weight resulted in similar changes. Immunostaining for TNF-bp revealed positivity in the apical cytoplasm of renal tubular epithelium within 1 h of i.v. dosing. Immunostaining of kidneys from chronically dosed rats indicated that protein was present in some vacuoles as long as dosing continued; however, kidneys from animals on a reversibility study

had vacuoles but no immunostaining for TNF-bp. These results, along with a study that showed more severe lesions with <code>PEG-linked</code> proteins of lower molecular weight and minimal if any lesions with <code>PEG-linked</code> proteins > 70 kDa, suggest that TNF-bp is filtered through the glomerulus and that the protein with attached PEG is reabsorbed by the proximal tubules. Vacuolation may be a result of fluid distension of lysosomes due to the hygroscopic nature of PEG. These studies demonstrated that <code>PEG-linked</code> proteins have the capacity to induce renal tubular vacuolation at high doses. However, the change was not associated with alteration of clinical pathology or functional markers.

- L49 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN

  AB A review with 8 refs. of the influence of pegylation conditions and

  PEG linker quality on attachment of PEG to

  protein cysteine residues, and of the influence of NaBH3CN quality and PEG aldehyde quality on PEG modification of protein amino groups.
- L49 ANSWER 4 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 2
- Hydrazide derivatives of poly(ethylene glycol) (PEG-Hz) have a number AB of attributes making them useful for preparation of conjugates, particularly of polypeptides and glycoproteins. They form conjugates in mildly acidic aqueous solutions via two modes of reactivity. The first one involves hydrazone formation with reactive carbonyls generated on the substrate molecule by several different methods. These include oxidation of oligosaccharide residues of glycoproteins, glyoxylate / Cu2+ -mediated transamination of the N-terminal residue of polypeptides, periodate oxidation of N-terminal Ser or Thr residues. The second mode involves coupling with cardodiimide-activated carboxyl groups forming diacylhydrazide linkages with PEG. Synthesis of PEG-Hz is straightforward by hydrazinolysis of esters of either carboxymethylated PEG or urethane-linked amino acid. Having an unusual amino acid, e.g. beta-Ala, as part of the linker offers a convenient way for composition determination of protein conjugates, particularly those containing multiple chains of mPEG-O(C=O)-beta-Ala-Hz, by amino acid analysis. Our work involving PEG-Hz conjugation, including examples of preparation of N-terminally modified polypeptides, oligosaccharide-linked glycoproteins, polypeptides modified on their carboxyl groups, and immunoconjugates of enzymes and liposomes is discussed in this review.
- L49 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN AB In this presentation we describe two applications of new hydrolytically-degradable PEG derivs. The first involves preparation and characterization of degradable PEG hydrogels. These PEGs contain ester linkages and can be prepared by reaction of PEG carboxylic acids with PEG. The degradation rates of these gels can be fine-tuned by variation in mol. structure of the esters and in the degree of branching of the PEGs. The second application involves preparation of soluble PEGprotein conjugates in which the PEG is attached to the protein via a hydrolytically degradable ester linkage. The ester-containing PEGs are prepared by condensation of PEG carboxylic acids with small hydroxy-acids. Conversion to succinimidyl active esters permits coupling to amino groups of proteins. Varying the types of PEG acid and hydroxy-acid gives control over the rates of hydrolysis. Applications to drug delivery will be presented.
- ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3

  AB The present invention relates to pegylyated proteins, including modified Ig mols. mildly derivatized with polyethylene glycol. The pegylyated Igs also contains a T cell epitope or a B cell epitope. Such "pegylated" Igs may be used to produce an enhanced immune response in the absence of adjuvant. In particular embodiments, the present invention relates to

proteins conjugated to polyethylene glycol via carbohydrate residues.

- L49 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
  AB Physiol. active proteins, e.g., superoxide dismutase, are optimized for pharmaceutical use by covalently linking with a low diol polyalkylene oxide, e.g., polyethylene glycol, to increase their half-life and reduce immunogenicity. Also disclosed is a method of treatment of disease processes associated with the adverse effects on tissue of superoxide anions, such as ischemic events, reperfusion
  - increase their half-life and reduce immunogenicity. Also disclosed is a method of treatment of disease processes associated with the adverse effects on tissue of superoxide anions, such as ischemic events, reperfusion injury, trauma and inflammation. Preparation of methoxypolyethylene glycol N-succinimidyl succinate and its use for modifying superoxide dismutase, catalase, etc., were shown.
- L49 ANSWER 8 OF 20 MEDLINE on STN DUPLICATE 4
- AB A novel **PEG linker** that employs a thiazolidine-2thione group has been synthesized. Kinetic studies done on this compound
  demonstrate a relatively long half-life compared to those of traditional
  succinimidyl linkers. This new PEG derivative reacts with proteins under
  mild conditions and was utilized to conjugate bovine hemoglobin (bHb) to
  provide a **PEG** amide-linked protein. The physical
  characteristics of this conjugate were compared with those of the known **PEG** carbamate-linked bHb.
- L49 ANSWER 9 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
- AB Purpose. Recombinant human granulocyte-colony stimulating factor (rhG-CSF) was covalently conjugated to both rat and human serum albumin (RSA and HSA respectively) to increases the circulating half life (t(1/2)) of rhG-CSF.

Methods. Conjugates of RSA (MW 67,000) and HSA (MW 66,000) were prepared by linking the two proteins through a heterobifunctional maleimido-carboxyl polyethylene glycol (PEG) and were tested in the rat. The conjugates were injected intravenously (IV) at the equivalent dose of 50 mu g/kg of rhG-CSF, and white blood cell (WBC) counts and plasma concentrations of drug were determined. A comparison of pharmacokinetic parameters was made between rhG-CSF, the conjugates RSA-PEG-rhC-CSF and HSA-PEG-rhG-CSF, and a non-covalent mixture of rhG-CSF and HSA.

Results. The albumin-rhG-CSF conjugates are eliminated more slowly from the circulation. The clearance values are reduced from 0.839 +/- 0.121 ml/min/kg for rhG-CSF to 0.172 +/- 0.013 ml/min/kg for RSA-PEG-rhG-CSF and 0.141 +/- 0.005 ml/min/kg for HSA-PEG-rhG-CSF. WBC counts increased in both absolute number and duration as compared to rhc-CSF alone. The albumin rhG-CSF conjugates had enhanced serum stability relative to free rhG-CSF. The rate of degradation of the albumin conjugates incubated in rat Serum at 37 degrees C decreased five fold.

Conclusions. The results from the study show that specific conjugation of rhG-CSF to albumin decreases plasma clearance in vivo, causes increased WBC response, and increases serum stability as compared to free rhG-CSF.

- L49 ANSWER 10 OF 20 MEDLINE on STN DUPLICATE 5
- AB The first examples of **PEG linkers** containing the highly fluorescent dansyl group have been synthesized. Quantum yields of these **PEG** fluorescent **linkers** (PFL) were determined and utilized in calculating the **PEG** number of various **protein conjugates.** The method was also shown to be applicable to lower molecular weight drugs as exemplified by taxol.
- L49 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN

  AB Covalent attachment of polyethylene glycol (PEG) to proteins increases plasma half life, increases resistance to proteolysis and reduces antigenicity/ immunogenicity. Such benefits have prompted the development of PEG-proteins as therapeutic agents. A novel method of activating PEG

with tresyl chloride, which attaches **PEG** to amino groups by a direct secondary amine **linkage**, without any coupling moiety (portion of the activated **PEG**) remaining in the PEG-protein construct have been investigated. Using erythropoietin and granulocyte-macrophage colony stimulating factor as the target proteins, this method has been compared with four other common methods of PEG activation: cyanuric acid, phenylchloroformate, carbonyldiimidazole and succinimidyl succinate. Either conservation of biol. activity or lack of toxic contaminants (or both) was inferior for the other methods.

L49 ANSWER 12 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

Liposome aggregation is a major problem associated with the covalent AB attachment of proteins to liposomes. This report describes a procedure for coupling proteins to liposomes that results in little or no change in liposome size. This is achieved by incorporating appropriate levels of poly(ethylene glycol)-modified lipids into the liposomes. The studies employed thiolated avidin-D coupled to liposomes containing the thio-reactive lipid N-(4-(p-maleimidophenyl)butyryl)dipalmitoyl phosphatidylethanolamine (1 mol % of total lipid) and various amounts of MePEG-S-POPE (monomethoxypoly(ethylene glycol) linked to phosphatidylethanolamine via a succinate linkage). The influence of PEG chain length and density was also assessed. The presence of PEG on the surface of liposomes is shown to provide an effective method of inhibiting aggregation and the corresponding increase in liposome size during the covalent coupling of avidin-D. A balance between the size of the PEG used and the amount of PEG-lipid incorporated into the liposome had to be achieved in order to maintain efficient coupling. Optimal coupling efficiencies in combination with minimal aggregation effects were achieved using 2 mol % MePEG(2000)-S-POPE (PEG of 2000 MW) or 0.8 mol % MePEG(5000)-S-POPE (PEG of 5000 MW). At these levels, the presence of PEG did not affect the biotin binding activity of the covalently attached avidin. The ability of the resulting liposomes to specifically target to biotinylated cells is demonstrated.

ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN

Compds. for modifying polypeptides with PEG or other water-soluble organic polymers are described. The water-soluble polymer reagents include hydrazine, hydrazine carboxylate, semicarbazole, thiosemicarbazide, carbonic acid dihydrazide, carbazide, thiocarbazide, and arylhydrazide derivs. as well as oxylamine derivs. of water-soluble organic polymers, such as polyethylene glycol, polypropylene glycol, polyoxyethylated polyol, heparin, heparin fragments, dextran polysaccharides, polyamino acids, and polyvinyl alc. Kits for modifying polypeptides with the above water-soluble polymer reagents are also provided. Thus, erythropoietin was modified by oxidation and treatment with monomethoxypolyoxyethylene semicarbazide and the product was separated by chromatog. The antigenicity and the effect on hematocrit levels of the above derivs. were demonstrated.

L49 ANSWER 14 OF 20 MEDLINE on STN DUPLICATE 6 Covalent attachment of poly(ethylene glycol) (PEG) to proteins produces conjugates with altered/improved physicochemical and biological properties which depend upon the number of PEG chains linked. Ouantification of the attached PEG is however not a trivial issue. The partition coefficient, K, of the PEG-protein conjugate in PEG/dextran two-phase systems provides a quantitative measure for the degree of modification. A linear relationship between log K and the number of PEG chains was observed in fractionated PEG-modified-granulocyte-macrophage colony stimulating factor conjugates having 1 to 3 substitutions. Furthermore, in mixtures of PEG-bovine-serum-albumin conjugates with increasing degrees of modification, a linear relationship was found between log K and n, the average substitution. The increment in log K per PEG chain added is protein specific and this suggests that the interactions between the PEG-

protein conjugate and the polymers in the phase system are more complex than just a simple affinity of the PEG for the PEG-rich top phase. Increasing the polymer concentration in the phase system produces larger increments in log K per PEG molecule attached and the proportionality between log K and number of PEG molecules is only compromised for conjugates with high degree of substitution when partitioned in biphasic systems of high concentration of polymers.

L49 ANSWER 15 OF 20 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

AB US 5252714 A UPAB: 19931202

Polyalkylene glycol derivs. of formula R1(CH2)2X(CH2)mX(CH2)2(OC(R2)HCH2)n

X(CH2)mX(CH2)2R3 (I) are new. R1 and R3=CHO, CH=NR4 or CH2NHR4; R4=an

antibody; X=O or S; R2=H or 1-6C alkyl; n=an integer less than 10,000;

m=2-6

Also claimed is a process for amine modification comprising preparing an 'amine comprising substance' (II) in a solution and adding a cpd. (I; R1=R3=CHO).

USE/ADVANTAGE - Cpds. (I; R1=R3=CHO) may be used (a) to prepare polyalkylene glycol conjugates of proteins, especially antibodies, i.e. cpds. (I) where R1 and/or R3=CH=NR4 or CH2NHR4, and (b) to link such proteins to aminated surfaces. In contrast to known reactive polyethylene glycol (PEG) derivs., PEG derivs. of type (I; R1=R3=CHO) are not destroyed by water, are reactive in aqueous media, and react selectively with amino gps.

Dwg. 0/0

- ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN

  Base treatment of polyethylene glycol-derivatized superoxide dismutase in which the polyethylene glycol is linked to the protein via a succinyl bridge, removes the polyethylene glycol leaving a succinyl marker.

  Exhaustive succinylation with d4-succinic anhydride completes the derivatization in order to minimize fractionation in proteolysis, chromatog.; and desorption in the mass spectrometer. Production of peptides from the derivatized protein for high-resolution and high-resolution tandem MS allows identification of the site that had been derivatized by polyethylene glycol and the determination of the amount of polyethylene glycol originally at each site. The mass spectrometric strategy outlined herein can be applied to other proteins derivatized for therapeutic administration.
- L49 ANSWER 17 OF 20 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
- AB Novelty: Novel polyethylene glycol (PEG)
  conjugates of proteins produced by using unique
  linkers which connect the various free amino acid groups in a
  protein to PEG which circumvent the problems associated with the formation
  of other PEG protein conjugates. The protein
  interleukin-1 receptor antagonist (IL-1ra) and interleukin-1 (IL-1)
  conjugated to PEG are also provided. Biology: The PEG protein
  conjugates are physiologically active, substantially
  non-immunogenic and water-soluble having at least part of the biological
  activity of the protein which forms the conjugate.
  Chemistry: The conjugate of a protein is produced by
  condensing activated PEG (PEG wherein one hydroxy group has been
  replaced by an activated linker) with one or more of the free
  amino groups of the protein.
- ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN

  Biol. active polypeptides and glycopolypeptides are conjugated at a reactive carbonyl or carboxylic acid group of the polypeptide with water-soluble polymers by a linkage containing a hydrazide or hydrazone functional group. The linkage preferably also includes an amino acid or peptide sequence. The conjugates represent a novel form of drug delivery

(no data). Methoxy-PEG (mPEG) was treated with phosgene and then reacted with  $\beta$ -alanine Et ester.HCl. The mPEG- $\beta$ -alanine Et ester product was treated with hydrazine under reflux for 6 h and the mPEG-hydrazide derivative containing  $\beta$ -Ala was **conjugated** to various **proteins**, e.g. activated chymotrypsin, activated bovine serum albumin, oxidized ovalbumin, oxidized human IgG, and activated G-CSF. The proteins were activated at the carboxyl groups with EDC (carbodimide) or N-hydroxy-5-norbornene-2,3-dicarboximide. Carbohydrate groups were oxidized with NaIO4 for activation. Extensive crosslinking of the proteins was prevented.

L49 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN AB A bone growth factor, such as the transforming growth factor- $\beta$  (TGF- $\beta$ ), activin and bone morphogenetic **protein**, are **conjugated** a targeting mol. with bone affinity (tetracycline, calcein, bisphosphonate, estrogen, etc.). Conjugation is carried out using a cross-linker, preferably a synthetic hydrophilic polymer, such as **PEG.** A solution of 2  $\mu$ mol tetracycline in 1  $\mu$ mol bisepoxy-PEG was heated at 90°, followed by the addition of a solution of 100  $\mu$ g TFF- $\beta$ 2 in 0.02 M Na borate containing 0.02% SDS and 50% acetonitrile and pH adjustment to 9, to give the TGF- $\beta$ -PEG-tetracycline conjugate.

L49 ANSWER 20 OF 20 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 7

AB A new type of functionalized derivatives of polyethylene glycol (PEG), namely succinimidyl carbonates (SC), were prepared and evaluated as reagents for preparation of PEG-protein conjugates.

SC-activated PEGs showed high reactivity towards amino groups of lysine residues producing under mild conditions (pH 7.0 - 10.0, 25-degrees-C, 30 min) extensively modified proteins, in which PEG chains are linked to a polypeptide core through stable urethane (carbamate) linkages. A variety of proteins: chymotrypsin, trypsin, adenosine deaminase, asparaginase, arginase, hemoglobin were subjected to modifications with SC-PEG yielding conjugates with excellent preservation of biological/enzymatic activities.

=> log y		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	109.12	126.86
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-6.57	-6.57

STN INTERNATIONAL LOGOFF AT 08:51:56 ON 20 APR 2005

FILE 'HOME' ENTERED AT 15:21:13 ON 20 APR 2005

=> fil .bec COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS, ESBIOBASE, BIOTECHNO, WPIDS' ENTERED AT 15:21:21 ON 20 APR 2005 ALL COPYRIGHTS AND RESTRICTIONS APPLY. SEE HELP USAGETERMS FOR DETAILS.

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=> s peg or polyethylene glycol
 FILE 'MEDLINE'
           8959 PEG
          33678 POLYETHYLENE
          22000 GLYCOL
           9086 POLYETHYLENE GLYCOL
                  (POLYETHYLENE (W) GLYCOL)
 L1
          14753 PEG OR POLYETHYLENE GLYCOL
 FILE 'SCISEARCH'
          14973 PEG
          49789 POLYETHYLENE
          36174 GLYCOL
          11455 POLYETHYLENE GLYCOL
                  (POLYETHYLENE (W) GLYCOL)
 L2
          21749 PEG OR POLYETHYLENE GLYCOL
 FILE 'LIFESCI'
           2228 PEG
           4480 "POLYETHYLENE"
           5906 "GLYCOL"
           3000 POLYETHYLENE GLYCOL
                  ("POLYETHYLENE" (W) "GLYCOL")
 L3
           4068 PEG OR POLYETHYLENE GLYCOL
 FILE 'BIOTECHDS'
           6044 PEG
           3945 POLYETHYLENE
           4515 GLYCOL
           3036 POLYETHYLENE GLYCOL
                  (POLYETHYLENE (W) GLYCOL)
 L4
           7723 PEG OR POLYETHYLENE GLYCOL
 FILE 'BIOSIS'
          11854 PEG
          23925 POLYETHYLENE
          32559 GLYCOL
          14532 POLYETHYLENE GLYCOL
                  (POLYETHYLENE (W) GLYCOL)
 L5
          20621 PEG OR POLYETHYLENE GLYCOL
 FILE 'EMBASE'
           8915 PEG
          18670 "POLYETHYLENE"
          28246 "GLYCOL"
           8533 POLYETHYLENE GLYCOL
                  ("POLYETHYLENE"(W) "GLYCOL")
 L6
          14197 PEG OR POLYETHYLENE GLYCOL
 FILE 'HCAPLUS'
          31703 PEG
         323028 POLYETHYLENE
         328789 GLYCOL
          90639 POLYETHYLENE GLYCOL
                  (POLYETHYLENE (W) GLYCOL)
         108449 PEG OR POLYETHYLENE GLYCOL
 L7
FILE 'NTIS'
            321 PEG
           5591 POLYETHYLENE
           1894 GLYCOL
            253 POLYETHYLENE GLYCOL
                   (POLYETHYLENE (W) GLYCOL)
```

499 PEG OR POLYETHYLENE GLYCOL

L8

```
3672 PEG
          4796 POLYETHYLENE
          6391 GLYCOL
          3005 POLYETHYLENE GLYCOL
                 (POLYETHYLENE (W) GLYCOL)
L9
          5248 PEG OR POLYETHYLENE GLYCOL
FILE 'BIOTECHNO'
          2816 PEG
          4665 POLYETHYLENE
          7260 GLYCOL
          3167 POLYETHYLENE GLYCOL
                 (POLYETHYLENE (W) GLYCOL)
L10
          4868 PEG OR POLYETHYLENE GLYCOL
FILE 'WPIDS'
         15802 PEG
        197943 POLYETHYLENE
        109036 GLYCOL
         26705 POLYETHYLENE GLYCOL
                 (POLYETHYLENE (W) GLYCOL)
L11
       39735 PEG OR POLYETHYLENE GLYCOL
TOTAL FOR ALL FILES
L12
        241910 PEG OR POLYETHYLENE GLYCOL
=> s (bifunctional or multifunctional)
FILE 'MEDLINE'
          6151 BIFUNCTIONAL
          7414 MULTIFUNCTIONAL
L13
         13490 (BIFUNCTIONAL OR MULTIFUNCTIONAL)
FILE 'SCISEARCH'
         10095 BIFUNCTIONAL
         10543 MULTIFUNCTIONAL
L14
         20478 (BIFUNCTIONAL OR MULTIFUNCTIONAL)
FILE 'LIFESCI'
          2477 BIFUNCTIONAL
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           372 MULTIFUNCTIONAL
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          6661 MULTIFUNCTIONAL
         12003 (BIFUNCTIONAL OR MULTIFUNCTIONAL)
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         17705 MULTIFUNCTIONAL
L19
         36209 (BIFUNCTIONAL OR MULTIFUNCTIONAL)
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FILE 'ESBIOBASE'

FILE 'NTIS'

249 BIFUNCTIONAL

528 MULTIFUNCTIONAL

L20 775 (BIFUNCTIONAL OR MULTIFUNCTIONAL)

FILE 'ESBIOBASE'

2806 BIFUNCTIONAL

4389 MULTIFUNCTIONAL

L21 7158 (BIFUNCTIONAL OR MULTIFUNCTIONAL)

FILE 'BIOTECHNO'

2812 BIFUNCTIONAL

3539 MULTIFUNCTIONAL

L22 6314 (BIFUNCTIONAL OR MULTIFUNCTIONAL)

FILE 'WPIDS'

5002 BIFUNCTIONAL

11126 MULTIFUNCTIONAL

L23 16020 (BIFUNCTIONAL OR MULTIFUNCTIONAL)

TOTAL FOR ALL FILES

L24 132995 (BIFUNCTIONAL OR MULTIFUNCTIONAL)

=> s 124(5a)112

FILE 'MEDLINE'

L25 24 L13 (5A) L1

FILE 'SCISEARCH'

L26 39 L14(5A)L2

FILE 'LIFESCI'

L27 11 L15(5A)L3

FILE 'BIOTECHDS'

L28 11 L16(5A)L4

FILE 'BIOSIS'

L29 27 L17(5A)L5

FILE 'EMBASE'

L30 26 L18(5A)L6

FILE 'HCAPLUS'

L31 114 L19(5A)L7

FILE 'NTIS'

L32 1 L20(5A)L8

FILE 'ESBIOBASE'

L33 11 L21(5A)L9

FILE 'BIOTECHNO'

L34 15 L22(5A)L10

FILE 'WPIDS'

L35 31 L23(5A)L11

TOTAL FOR ALL FILES

L36 310 L24(5A) L12

=> s 136 and (link? or crosslink? or conjugat?)

FILE 'MEDLINE'

382837 LINK?

10817 CROSSLINK?

75574 CONJUGAT?

L37 18 L25 AND (LINK? OR CROSSLINK? OR CONJUGAT?)

FILE 'SCISEARCH'

411725 LINK?

28041 CROSSLINK?

106571 CONJUGAT?

L38 24 L26 AND (LINK? OR CROSSLINK? OR CONJUGAT?)

FILE 'LIFESCI'

128013 LINK?

4165 CROSSLINK?

22489 CONJUGAT?

L39 7 L27 AND (LINK? OR CROSSLINK? OR CONJUGAT?)

FILE 'BIOTECHDS'

30772 LINK?

2898 CROSSLINK?

8285 CONJUGAT?

L40 8 L28 AND (LINK? OR CROSSLINK? OR CONJUGAT?)

FILE 'BIOSIS'

340098 LINK?

14929 CROSSLINK?

84018 CONJUGAT?

L41 17 L29 AND (LINK? OR CROSSLINK? OR CONJUGAT?)

FILE 'EMBASE'

339891 LINK?

11291 CROSSLINK?

72830 CONJUGAT?

L42 18 L30 AND (LINK? OR CROSSLINK? OR CONJUGAT?)

FILE 'HCAPLUS'

418245 LINK?

249495 CROSSLINK?

207032 CONJUGAT?

L43 55 L31 AND (LINK? OR CROSSLINK? OR CONJUGAT?)

FILE 'NTIS'

32483 LINK?

3105 CROSSLINK?

4589 CONJUGAT?

L44 1 L32 AND (LINK? OR CROSSLINK? OR CONJUGAT?)

FILE 'ESBIOBASE'

144684 LINK?

4417 CROSSLINK?

25047 CONJUGAT?

L45 9 L33 AND (LINK? OR CROSSLINK? OR CONJUGAT?)

FILE 'BIOTECHNO'

173624 LINK?

4956 CROSSLINK?

24320 CONJUGAT?

L46 10 L34 AND (LINK? OR CROSSLINK? OR CONJUGAT?)

FILE 'WPIDS'

444068 LINK?

77310 CROSSLINK?

44496 CONJUGAT?

L47 21 L35 AND (LINK? OR CROSSLINK? OR CONJUGAT?)

TOTAL FOR ALL FILES

=> s 148 not 1999-2005/py

FILE 'MEDLINE'

3325502 1999-2005/PY

L49 5 L37 NOT 1999-2005/PY

FILE 'SCISEARCH'

6385167 1999-2005/PY

L50 8 L38 NOT 1999-2005/PY

FILE 'LIFESCI'

647543 1999-2005/PY

L51 3 L39 NOT 1999-2005/PY

FILE 'BIOTECHDS'

126993 1999-2005/PY

L52 0 L40 NOT 1999-2005/PY

FILE 'BIOSIS'

3277108 1999-2005/PY

L53 5 L41 NOT 1999-2005/PY

FILE 'EMBASE'

2914482 1999-2005/PY

L54 5 L42 NOT 1999-2005/PY

FILE 'HCAPLUS'

6178020 1999-2005/PY

L55 15 L43 NOT 1999-2005/PY

FILE 'NTIS'

108997 1999-2005/PY

L56 1 L44 NOT 1999-2005/PY

FILE 'ESBIOBASE'

1817014 1999-2005/PY

L57 1 L45 NOT 1999-2005/PY

FILE 'BIOTECHNO'

611346 1999-2005/PY

L58 4 L46 NOT 1999-2005/PY

FILE 'WPIDS'

5325720 1999-2005/PY

L59 1 L47 NOT 1999-2005/PY

TOTAL FOR ALL FILES

L60 48 L48 NOT 1999-2005/PY

=> dup rem 160

PROCESSING COMPLETED FOR L60

L61 21 DUP'REM L60 (27 DUPLICATES REMOVED)

=> d tot

L61 ANSWER 1 OF 21 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 1

TI An Os(byp)(2)ClPyCH(2)NHpoly(allylamine) hydrogel mediator for enzyme wiring at electrodes

SO ELECTROCHIMICA ACTA, (JAN 1998) Vol. 43, No. 23, pp. 3525-3531.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE,
KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
ISSN: 0013-4686.

- AU Danilowicz C (Reprint); Corton E; Battaglini F; Calvo E J
- AN 1998:675541 SCISEARCH
- L61 ANSWER 2 OF 21 MEDLINE on STN DUPLICATE 2
- Combined use of carboxyl-directed protein pegylation and vector-mediated blood-brain barrier drug delivery system optimizes brain uptake of brain-derived neurotrophic factor following intravenous administration.
- SO Pharmaceutical research, (1998 Apr) 15 (4) 576-82. Journal code: 8406521. ISSN: 0724-8741.
- AU Pardridge W M; Wu D; Sakane T
- AN 1998249553 MEDLINE
- L61 ANSWER 3 OF 21 MEDLINE on STN DUPLICATE 3
- TI Amino acids and peptides. XXXIII. A bifunctional poly(ethylene glycol) hybrid of laminin-related peptides.
- SO Biochemical and biophysical research communications, (1998 Jul 30) 248 (3) 485-9.
  - Journal code: 0372516. ISSN: 0006-291X.
- AU Maeda M; Kawasaki K; Mu Y; Kamada H; Tsutsumi Y; Smith T J; Mayumi T
- AN 1998369575 MEDLINE
- L61 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Nonimmunogenic MHC-blocking peptides
- SO PCT Int. Appl., 37 pp.
  - CODEN: PIXXD2
- IN Wiley, Don C.; Bouvier, Marlene
- AN 1997:145226 HCAPLUS
- DN 126:139883
- PATENT NO. KIND DATE APPLICATION NO. DATE

  -----PI WO 9700084 A1 19970103 WO 1996-US10396 19960614

  W: CA, JP, US

  RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
- L61 ANSWER 5 OF 21 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Immobilisation and release of hydroxylic compounds, e.g. oligo nucleotide(s) using linker compound containing protected amine which, when deprotected, attacks intramolecular phosphate tri ester.
- PI US 5688940 A 19971118 (199801)\* 9 C07H021-00
- IN LYTTLE, M H
- L61 ANSWER 6 OF 21 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
- TI Phospholipid derivatized with peg bifunctional linker and liposome containing it.
- Official Gazette of the United States Patent and Trademark Office Patents, (Sept. 17, 1996) Vol. 1190, No. 3, pp. 2098. print. CODEN: OGUPE7. ISSN: 0098-1133.
- AU Tagawa, T. [Inventor]; Awane, K. [Inventor]; Nagaike, K. [Inventor]
- AN 2002:49522 BIOSIS
- L61 ANSWER 7 OF 21 MEDLINE on STN DUPLICATE 4
- TI Interactions and applications of soluble heterobifunctional affinity chelating polymers in immobilized metal affinity chromatography.
- SO Journal of molecular recognition : JMR, (1996 Sep-Dec) 9 (5-6) 733-7. Journal code: 9004580. ISSN: 0952-3499.
- AU Ehteshami G; Porath J; Guzman R
- AN 97317982 MEDLINE
- L61 ANSWER 8 OF 21 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 5
- TI FIBROBLAST AGGREGATION BY SUSPENSION WITH CONJUGATES OF POLY(ETHYLENE GLYCOL) AND RGD
- SO BIOTECHNOLOGY AND BIOENGINEERING, (20 MAY 1996) Vol. 50, No. 4, pp. 349-356.

- ISSN: 0006-3592.
- AU DAI W G; SALTZMAN W M (Reprint)
- AN 96:326901 SCISEARCH
- L61 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Kinetics and mechanisms of multifunctional monomer photopolymerizations
- SO Polymeric Materials Science and Engineering (1996), 75, 202-203 CODEN: PMSEDG; ISSN: 0743-0515
- AU Anseth, Kristi S.
- AN 1996:498087 HCAPLUS
- DN 125:168731
- L61 ANSWER 10 OF 21 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
- TI CROSS-LINKED POLY(ETHYLENE OXIDE) FOR DRUG-RELEASE SYSTEMS
- SO MACROMOLECULAR SYMPOSIA, (JAN 1996) Vol. 103, pp. 193-211. ISSN: 1022-1360.
- AU BELCHEVA N (Reprint); STAMENOVA R; TSVETANOV C; LAMBOV N; TSANKOV S; SMID
- AN 96:151445 SCISEARCH
- L61 ANSWER 11 OF 21 LIFESCI COPYRIGHT 2005 CSA on STN
- TI Phospholipid derivatized with PEG bifunctional
- linker and liposome containing it
- SO (19960917) . US Patent 5556948; US Cl. 530/391.9 424/178.1 424/450 530/391.1 548/119.
- AN 97:108487 LIFESCI
- L61 ANSWER 12 OF 21 NTIS COPYRIGHT 2005 NTIS on STN
- TI Multifunctional Acrylates and the Synthesis Thereof. Patent.
- NR PB95-178448/XAB; PAT-APPL-7-828 316, PATENT-5 380 901
  - 7p; Filed 30 Jan 92, patented 10 Jan 95
- PD 19950110
- AU Antonucci, J. M.; Stansbury, J. W.; Cheng, G. W.
- AN 1995(17):03702 NTIS
- L61 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Gels containing cells for augmenting tissues
- SO PCT Int. Appl., 31 pp.
  - CODEN: PIXXD2
- IN Estridge, Trudy D.; Rao, Prema R.
- AN 1995:969690 HCAPLUS
- DN 123:350408

21,	PATENT NO.			KIND		DATE			APPLICATION NO.					DATE					
			<b></b>	<del>-</del>			-						<del>-</del>			-			
ΡI	WO	9526	761			A1		1995	1012		WO 1	.995-	US39	91		. 15	9950	331	
								, MX,											
		RW:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	ΝL,	PT,	SE	
	CA	2187				AΑ		1995				.995-					9950		
	AU	9522	029			A1		1995	1023		AU 1	1995-	2202	9		1	9950	331	
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	JΡ	1050	1706			T2		1998	0217		JP 1	L995-	5258	55		1:	9950	331	

- L61 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Activity and Stability of Enzymes Incorporated into Acrylic Polymers
- SO Journal of the American Chemical Society (1995), 117(17), 4843-50 CODEN: JACSAT; ISSN: 0002-7863
- AU Yang, Zhen; Mesiano, Anita J.; Venkatasubramanian, Srikanth; Gross, Susan H.; Harris, J. Milton; Russell, Alan J.
- AN 1995:520854 HCAPLUS
- DN 123:78410

- L61 ANSWER 15 OF 21 MEDLINE on STN . DUPLICATE (
- TI Cell-binding peptides conjugated to poly(ethylene glycol) promote neural cell aggregation.
- SO Bio/technology (Nature Publishing Company), (1994 Aug) 12 (8) 797-801. Journal code: 8309273. ISSN: 0733-222X.
- AU Dai W; Belt J; Saltzman W M
- AN 94318246 MEDLINE
- L61 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Novel heterobifunctionalized polystyrene-polyethylene glycol resin for simultaneous preparation of free and immobilized peptides and biological activity detected by confocal microscopy
- SO Letters in Peptide Science (1994), 1(3), 117-26 CODEN: LPSCEM; ISSN: 0929-5666
- AU Fleckenstein, Burkhard; Wiesmueller, Karl-Heinz; Brich, Manfred; Jung, Guenther
- AN 1995:390436 HCAPLUS
- DN 122:315066
- L61 ANSWER 17 OF 21 MEDLINE on STN DUPLICATE 7
- TI AUR Memorial Award 1993. A drug system (PDH) for interventional radiology. Synthesis, properties, and efficacy.
- SO Investigative radiology, (1993 Dec) 28 (12) 1083-9. Journal code: 0045377. ISSN: 0020-9996.
- AU Weissleder R; Bogdanov A; Frank H; Nossiff N; Bogdanova A; Schaffer B K; Brady T; Wittenberg J
- AN 94140526 MEDLINE
- L61 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI A crosslinked polyether solid electrolyte film made by one-step reaction at room temperature
- SO Gaofenzi Cailiao Kexue Yu Gongcheng (1993), 9(5), 122-6 CODEN: GCKGEI; ISSN: 1000-7555
- AU Xia, Duwei; Zhang, Zhaoxi; Hou, Xinping
- AN 1994:299924 HCAPLUS
- DN 120:299924
- L61 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Novel hydrophilic and hydrophobic acrylic monomers and oligomers for dental and medical applications
- SO Polymer Preprints (American Chemical Society, Division of Polymer Chemistry) (1992), 33(2), 522-3 CODEN: ACPPAY; ISSN: 0032-3934
- AU Antonucci, J. M.; Sansbury, J. W.; Cheng, G. W.
- AN 1994:165612 HCAPLUS
- DN 120:165612
- L61 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Preparation of polyethylene glycol derivatives with two different functional groups at the termini
- SO Polymer Preprints (American Chemical Society, Division of Polymer Chemistry) (1986), 27(1), 1-2
  CODEN: ACPPAY; ISSN: 0032-3934
- AU Zalipsky, Shmuel; Barany, George
- AN 1986:406904 HCAPLUS
- DN 105:6904
- L61 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
- TI Combustion inhibitor for gas-producing charges
- IN Bohn, James N.; Sandhoff, Allan G.
- AN 1959:14076 HCAPLUS
- DN 53:14076
- OREF 53:2627a-c,2628a

=> d ab 3,20

DUPLICATE 3 L61 ANSWER 3 OF 21 MEDLINE on STN A novel amino acid type poly(ethylene glycol) (aaPEG) was prepared and its application as a drug-carrier was examined. The peptides, Pro-Asp-Ser-Gly-Arg (PDSGR) and Tyr-Ile-Gly-Ser-Arg (YIGSR) which are active fragments of Laminin (a cell adhesion protein), were previously reported to be inhibitors of experimental metastasis. Both peptides were conjugated with aaPEG (average molecular weight, 3,000) to prepare a bifunctional peptide-PEG hybrid. The hybrid, PDSGR-aaPEG-YIGSR, was manually prepared by the solid-phase fluorenylmethyloxycarbonyl (Fmoc) strategy. The antimetastatic activity of the peptides in mice was not lost when conjugated to form a larger aaPEG molecule. YIGSR(375 nmol) and PDSGR (375 nmol and 750 nmol) did not demonstrate antimetastatic activity, but a mixture of PDSGR (187 nnmol) and YIGSR (187 nmol) exhibited an inhibitory effect. The inhibitory effect of the hybrid (187 nmol) was more potent than that of the mixture (PDSGR and YIGSR), indicating that the inhibitory effect of the peptides was potentiated by hybrid formation with aaPEG.

AB Bifunctional polyethylene glycol (I) was treated with SOCl2 and pyridine in PhMe to give chlorinated I, which was treated with Et isocyanatoacetate in the presence of Et3N. The polymer product was treated with NaN3, saponified, and separated on a column containing DEAE-Sephadex in the tetraborate form to give N3(CH2CH2O)nCO2NHCH2CO2H [102778-01-8], which was dissolved in a 4:1 EtOH-CH2Cl2 mixture After adding 10% Pd/C, the mixture was hydrogenated overnight at 50 psi to give H2N(CH2CH2O)nCO2NHCH2CO2H, which was treated with N,N-diisopropyl ethylamine and di-tert-Bu pyrocarbonate to give tert-BuO2CNH(CH2CH2O)nCO2NHCH2CO2H [102778-02-9]. Use of the polymers in peptide synthesis and the preparation of protein conjugates and polymeric drugs was discussed.

=> s heterofunctional
FILE 'MEDLINE'

L62 29 HETEROFUNCTIONAL

FILE 'SCISEARCH'

L63 118 HETEROFUNCTIONAL

FILE 'LIFESCI'

L64 10 HETEROFUNCTIONAL

FILE 'BIOTECHDS'

L65 15 HETEROFUNCTIONAL

FILE 'BIOSIS'

L66 34 HETEROFUNCTIONAL

FILE 'EMBASE'

L67 25 HETEROFUNCTIONAL

FILE 'HCAPLUS'

L68 298 HETEROFUNCTIONAL

FILE 'NTIS'

L69 7 HETEROFUNCTIONAL

FILE 'ESBIOBASE'

L70 19 HETEROFUNCTIONAL

FILE 'BIOTECHNO'

L71 17 HETEROFUNCTIONAL

FILE 'WPIDS'

L72 52 HETEROFUNCTIONAL

TOTAL FOR ALL FILES

L73 624 HETEROFUNCTIONAL

=> s 112 and 173

FILE 'MEDLINE'

L74 8 L1 AND L62

FILE 'SCISEARCH'

L75 10 L2 AND L63

FILE 'LIFESCI'

L76 0 L3 AND L64

FILE 'BIOTECHDS'

L77 1 L4 AND L65

FILE 'BIOSIS'

L78 5 L5 AND L66

FILE 'EMBASE'

L79 5 L6 AND L67

FILE 'HCAPLUS'

L80 21 L7 AND L68

FILE 'NTIS'

L81 0 L8 AND L69

FILE 'ESBIOBASE'

L82 3 L9 AND L70

FILE 'BIOTECHNO'

L83 4 L10 AND L71

FILE 'WPIDS'

L84 6 L11 AND L72

TOTAL FOR ALL FILES

L85 63 L12 AND L73

=> s 185 not 1999-2005/py

FILE 'MEDLINE'

3325502 1999-2005/PY

L86 1 L74 NOT 1999-2005/PY

FILE 'SCISEARCH'

6385167 1999-2005/PY

L87 2 L75 NOT 1999-2005/PY

FILE 'LIFESCI'

647543 1999-2005/PY

L88 0 L76 NOT 1999-2005/PY

FILE 'BIOTECHDS'

126993 1999-2005/PY

FILE 'BIOSIS'

3277108 1999-2005/PY

L90 1 L78 NOT 1999-2005/PY

FILE 'EMBASE'

2914482 1999-2005/PY

L91 1 L79 NOT 1999-2005/PY

FILE 'HCAPLUS'

6178020 1999-2005/PY

L92 3 L80 NOT 1999-2005/PY

FILE 'NTIS'

108997 1999-2005/PY

L93 0 L81 NOT 1999-2005/PY

FILE 'ESBIOBASE'

1817014 1999-2005/PY

L94 0 L82 NOT 1999-2005/PY

FILE 'BIOTECHNO'

611346 1999-2005/PY

L95 1 L83 NOT 1999-2005/PY

FILE 'WPIDS'

5325720 1999-2005/PY

L96 0 L84 NOT 1999-2005/PY

TOTAL FOR ALL FILES

L97 9 L85 NOT 1999-2005/PY

=> dup rem 197

PROCESSING COMPLETED FOR L97

L98 4 DUP REM L97 (5 DUPLICATES REMOVED)

=> d tot

L98 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

TI Incorporation of PEG-proteins into polymers.

SO Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (1997), POLY-182 Publisher: American Chemical Society, Washington, D. C. CODEN: 64AOAA

AU LeJeune, K. E.; Panza, J.; Russell, A. J.

AN 1997:164107 HCAPLUS

L98 ANSWER 2 OF 4 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 1

TI Incorporation of poly(ethylene glycol) proteins into polymers

SO ACS SYMPOSIUM SERIES, (FEB 1997) Vol. 680, pp. 134-144.
Publisher: AMER CHEMICAL SOC, 1155 SIXTEENTH ST NW, WASHINGTON, DC 20036.
ISSN: 0097-6156.

AU Panza J L (Reprint); LeJeune K E; Venkatasubramanian S; Russell A J

AN 1998:12667 SCISEARCH

L98 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 2

TI Selective production of hybridoma cells: antigenic-based pre-selection of B lymphocytes for electrofusion with myeloma cells:

SO Biochimica et biophysica acta, (1990 Dec 10) 1055 (3) 199-206. Journal code: 0217513. ISSN: 0006-3002.

AU Tomita M; Tsong T Y

AN 91091428 MEDLINE